The Use of Fluoride Varnish in Children: A Critical Review with Treatment Recommendations

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This paper expands upon the recent report of the expert panel commissioned by the American Dental Association's Council on Scientific Affairs by offering evidence-based clinical recommendations for professionally applied topical fluoride. The authors strongly support the panel's recommendation that clinicians should rely upon caries risk criteria for determining those children who will receive a topical fluoride treatment. In this paper, the authors will take a position that when clinicians have made a decision to use topical fluoride therapy, fluoride varnish should be the only consideration for children ages 0-6 and children of all ages who have special health care needs that limit their attention span and/or cooperation. The authors offer an accompanying rationale based on dosage reduction and efficacy, that fluoride varnish should be the topical fluoride of choice for children ages 6-12. The authors expand upon the recent panel recommendations by examining published clinical trials to determine the best clinical techniques for varnish use. The authors offer clinicians the following recommendations prior to varnish use: a pre-application rubber cup or tooth brush prophylaxis, the application of varnish to dry teeth and post-operative instructions to include both no tooth brushing and a soft diet for 12 hours.

Keywords: *fluoride varnish, children, caries, caries risk, caries reduction, Duraphat*
J Clin Pediatr Dent 32(4): 259–264, 2008

INTRODUCTION

Recently the Council on Scientific Affairs of the American Dental Association (ADA) convened an expert panel to develop evidence-based clinical recommendations for the use of professionally applied topical fluoride. These recommendations were published in the Journal of the American Dental Association (JADA) in August, 2006.[1] As one dimension of their undertaking, the panel provided a system for grading scientific evidence and a system used for classifying the strength of recommendations. They also provided caries risk criteria.[1] The panel's initiative focused on fluoride foams, gels and varnish (referred to hereafter as foams, gels and varnish). They cited evidence that varnish takes less time, creates less patient discomfort, and achieves greater patient acceptability than gel, especially in pre-school aged children.[1] For children at moderate and high risk for dental caries, the panel recommended the use of varnish for children less than six years of age and varnish or gel for those ages 6-18.

This paper will expand on the panel's recommendations with a specific focus on children ages 12 and under. Our purpose is five-fold. To 1) review what is known about the safety of varnish for children, 2) underscore that varnish should be the only topical fluoride used for children 0-3 as well as for children with special health care needs that limit their attention span and/or cooperation, 3) recommend that varnish be the topical fluoride of choice for children ages 3-12, 4) provide clinicians with best practice recommendations for the clinical techniques upon which to rely for varnish use in children, and finally 5) comment on the current state of varnish products on the marketplace today.

WHAT IS FLUORIDE VARNISH?

Fluoride varnish is a natural tree resin (colophony or rosin) containing concentrated fluoride. A key feature of varnish is the fact that the resin base in which the fluoride is suspended is ***tenacious in its adherence to teeth***, allowing prolonged fluoride-enamel interaction over time. Most fluoride varnish products contain 2.26% fluoride from a suspension of 5% sodium fluoride (NaF) in an alcoholic solution of natural varnish substances.[2]

Although it has been used extensively throughout Europe for over 25 years, varnish approval by the Federal Drug Administration (FDA), a regulatory agency of the United

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States government, was not granted until 1994.[3] Approved as a "device" for use as a cavity liner and desensitizing agent, the FDA considers varnish to fall into a category of drugs and devices that "present minimal risk and is (are) subject to the lowest level of regulation." [4] Because caries prevention is a drug claim and not a device, the use of varnish in dental caries prevention is considered "off label" by the FDA, a common practice in medicine.[3] When using drugs and devices "off-label," dentists and physicians must take responsibility for their patients' safety. Due to the extensive clinical trials conducted demonstrating the efficacy and safety of varnish, the product is supported by the American Dental Association. [5]

Safety and Adverse Outcomes

The ADA expert panel underscored the fact that varnish can be used safely with children, even those under age three. Because our recommendations also rely heavily on varnish's safety margin, the purpose of this section is to review this topic in more detail. The concentration of fluoride is about two times as high in 5% NaF varnish (22.6mg F-/ml) as in APF (12.3mg F-/ml) gel.

In distilling the data from three APF clinical trials, Clark and coworkers[6] estimated that the amount of fluoride with one APF application ranged from 4-8 ml, delivering 49.2-98.4 mg F- in the mouth. In distilling the data from four clinical trials using fluoride varnish, Beltrán-Aguilar[3] estimated that 0.3-0.5 ml of varnish is applied with one application, delivering 6.8-11.3 mg F- in the mouth. Additionally, a Canadian study[6] reported that less than 0.5ml of Duraphat is needed to treat 6-7 year-old children, a Swedish study[7] reported that 0.3 ml varnish is sufficient for preschool-aged children and a U.S. study[8] reported that less than 0.1 ml is needed to treat infants at risk for early childhood caries. Taken together, these studies make it clear that the amount of fluoride delivered with varnish is considerably less than with APF gel.

The probable toxic fluoride dose for a child weighing 20kg is approximately 100mg (5mg/kg).[2] While this amount of fluoride is more than would be expected to be used for children, limiting fluoride ingestion as much as practical is a prudent practice due to the potential for gastric irritation with swallowed fluoride products. A review of APF studies reveals that a range of 6.5-36 mg is ingested after an APF application.[6] In addition, the dose from a gel application is swallowed over a short period of time and can cause significant increases in plasma fluoride concentrations.[9] Regarding fluoride varnish, two studies[10,11] evaluating the amount of fluoride ingested from varnish application found that the ingestion of fluoride from Duraphat ranged from 5.0-5.2 mg with a 0.5 ml application. Because of the tenacious adherence of the varnish to the teeth, this smaller dose of fluoride is swallowed over a number of hours, with a barely detectable effect on plasma fluoride concentration. Thus, the possibility of nausea, vomiting, or other fluoride toxic reaction is eliminated.[10]

Studies evaluating the plasma fluoride concentrations and urinary fluoride concentration of topical fluoride treatments offer excellent insights to assess the amounts of fluoride swallowed by children. Following application of Duraphat in a Scandinavian investigation on four healthy children ages 4, 5, 12 and 14, the urinary fluoride concentration 12 hours after application was between 500-1100 micrograms, well below the toxic dose; [11] indeed, the urinary levels are comparable to those seen following the use of fluoridated toothpaste and fluoride tablets and they are considerably lower than those using fluoride gels.[3]

What adverse outcomes have been reported with varnish? Two cases of contact allergy to varnish (Duraphat) have been reported. The first caused dermatitis on a dental assistant's hand while the second caused stomatitis in a patient; both cases are believed to be related to the colophony base in the varnish.[12] Concerns about applying varnish to asthmatic children have been mentioned[13] and are included in varnish package inserts but no adverse outcomes with asthmatic children have been reported to date.

Although not studied systematically, two anecdotal safety observations are of interest. The School of Dentistry at the University of North Carolina at Chapel Hill (UNC-CH) has been using varnish for over 12 years as the standard of care for children and adolescents with no adverse outcomes reported. Also, fluoride varnish is applied routinely by trained physicians/nurses in North Carolina's statewide "Into the Mouth of Babes" program for children 0-36 months. Since 2000, more than 480,000 treatments have been performed with no adverse outcomes.

Topical Fluoride for Children Ages 0-3

Because of safety concerns regarding the use of gels and foams in children under age three, there are no reported data for children in this age group. In contrast, contemporary data for the efficacy of varnish for infants are beginning to emerge. A recent clinical study by Weintraub and colleagues[14] examined 376 children ages 6-44 months in a 24-month randomized controlled trial (RCT) using counseling alone, counseling and varnish (Duraphat) one time annually, or counseling and varnish application at six month intervals. The number of lesions increased in the children who received counseling only. The number of carious lesions decreased significantly with increased varnish applications. The pooled d(e/m)fs percent caries reduction ranged from 53-93% by treatment group. Children who received no varnish were more than two times as likely to develop decay as those who were assigned to the annual varnish group. Children who did not receive varnish were nearly four times as likely to develop tooth decay than those who got two treatments annually or four treatments over 24 months.

Recently Rozier and colleagues[15] reported more findings on the use of varnish (Duraphat) for infants and young children. The study examined the use of varnish in a medical office-based setting wherein office visits included a dental screening, preventive counseling, varnish application and referral as needed for children 6-42 months of age. Those who had four or more visits showed a reduction in caries-

related treatments of 38.9% in anterior teeth. It should be noted that under the conditions of this investigation, it was not possible to disentangle the caries inhibiting effects of the preventive counseling *versus* varnish application; however, it seems plausible that varnish played a key role in the study's outcome.

To summarize: Based on the available evidence including dose reductions and efficacy justifications, we advocate that varnish should be the only topical fluoride modality used for children ages 0-3. Because of safety concerns, we advocate further that varnish should also be the only modality used for children with special health care needs who exhibit attention span and/or cooperation problems.

Topical Fluoride for Children Ages 3-6

There is a paucity of evidence to support the efficacy and safety of gels in children under age six. Although Jiang and colleagues[16] reported reductions of 24% for APF foam in a study spanning 24 months, this topical fluoride modality needs additional study before it can be recommended.[1] Considering the foregoing, the ADA Panel recommended the use of varnish for children less than six years of age. This recommendation for varnish is strongly supported with evidence from a meta-analysis[17] which reported an overall caries reduction of 38% (DMFS/dmfs). The ADA Panel also relied upon a systematic review from the Cochrane Collaboration[18] that found reductions of 46% for permanent teeth and 33% for primary teeth. Although there have been other systematic reviews since the Cochrane review in 2002, the latter is the most contemporary for assessing the efficacy of varnish for children 3-6.

To summarize: Based on the available evidence including dose reductions and efficacy justification, we strongly support the panel's recommendation that varnish should be the topical fluoride of choice for children 3-6.

Topical Fluoride for Children ages 6-12

The ADA panel's recommendations offer clinicians the option to rely upon gel or varnish for those patients ages 6-18 for whom topical fluoride is to be applied. The authors recommend strongly that varnish also should be the fluoride of choice for those 6-12. The authors base this recommendation on two factors: 1) safety and 2) efficacy.

Safety: Fluoride gel can be used safely in this age group but its use requires a very careful technique aimed at limiting patient swallowing and one that requires careful evacuation of intraoral fluoride overflow from trays. It should be noted that gels should be applied for four minutes because "one minute gel application" has not been supported with clinical trial data.[1] Accordingly, gel must be in the patients mouth for a longer time, offering greater opportunity for patients to swallow the gel which can increase the risk of gastric irritation.

Efficacy: The efficacy data suggest that varnish is at least as effective as gels for children ages 6-12. This claim is based upon two systematic reviews by the Cochrane Collaboration,[18,19] one of which focuses on varnish and the other on gel. Although other systematic reviews have been published, these two are comparable in part because of the Cochrane Collaboration's inclusion criteria. Caries reductions for varnish were 46% [18] while reductions for gel were 28%.[19]

There is only one published study that compares gel versus varnish directly in the same clinical trial for children in the mixed dentition. Tewari and colleagues[20] evaluated the efficacy of Duraphat *versus* APF or NaF gel on 6½-12 year old children, using a strict application protocol and detailed post-operative instructions in a 54-month randomized controlled trial (RCT). After 30 months, they found a 74% caries reduction with Duraphat *versus* a 35% reduction for APF gel and a 26% reduction with NaF gel. Because of its reductions, this RCT will be examined more closely in a later section of this paper.

To summarize: Based on all available evidence relative to safety and efficacy, the authors advocate that varnish should be the topical fluoride of choice for patients ages 6-12.

Application Technique Considerations

There is considerable disagreement relative to the proper application technique for fluoride varnish.[2] Key questions include:

1) Should a professional prophylaxis be completed prior to fluoride varnish applications?
2) Should the varnish be applied to dry teeth or does it matter?
3) Should post-operative instructions be given and, if so, what?

To address these questions we completed a Medline search for literature available from 1970-2006, finding 22 studies available in English in the Health Science Library at the University of North Carolina at Chapel Hill. Of these 22 studies only eight met the Cochrane criteria,[18] which would exclude those with a split-mouth design, quasi- or non-randomization or non-blinded studies. These studies are illustrated in Table I.

Table I. Clinical Technique Summary for Reported Primary and Permanent Tooth Studies Meeting the Cochrane Criteria

Year	Study	Prophy-Rubber Cup	Prophy-Toothbrush	Dried Teeth	Dietary Instructions	Brushing Instructions
1975	Koch [21]	yes	no	yes	yes	yes
1979	Holm [22]	no	yes	not reported	yes	yes
1984	Holm [23]	yes	no	yes	yes	yes
1984	Modeer [24]	yes	no	yes	yes	yes
1985	Clark [6]	yes	no	yes	yes	yes
1990	Tewari [20]	yes	no	yes	yes	yes
1991	Frostell [25]	yes	no	yes	yes	yes
1997	Bravo [26]	not reported	not reported	yes	yes	yes

Should a professional prophylaxis be completed prior to fluoride varnish application?
Table I summarizes the tooth preparation techniques relied upon in eight studies that have examined varnish efficacy. Based on these findings, it appears that either a conventional or tooth brush prophylaxis prior to varnish application will be effective.

Should the varnish be applied to dry teeth or does it matter?
This question is intriguing because several manufacturers' instructions state that varnish can be placed on moist teeth; however, if one looks to published evidence, Koch's *in vitro* study[27] showed greater uptake of fluoride varnish on dry versus wet surfaces. This finding supports the theoretical assumptions because varnish is hydrophobic and as such it adheres tenaciously to dry teeth and is unaffected by saliva or water once on a dry tooth. Although this laboratory-based study on fluoride uptake supports the application of varnish to dry teeth, laboratory evidence does not always predict clinical findings; however, table I illustrates that the clinical evidence to date has been drawn almost exclusively from studies where teeth have been dried prior to varnish placement. It should be noted that all of the studies included in the Cochrane analysis placed the varnish on dry teeth. These findings make a strong case for drying the teeth prior to varnish application.

What, if any, post-operative instructions should be given?
Table I summarizes both post-operative and brushing and dietary instructions for the eight studies listed. It is clear the preponderance of studies relied on both post-op brushing and dietary instructions. Again, it is noteworthy that the studies included in the Cochrane Review all relied upon both dietary and post-operative brushing instructions. Of special note is the Tewari study,[20] showing a caries reduction of 74.4% using strict post-operative instructions for brushing and dietary intake.

To summarize on technique considerations for children in a dental office environment: the clinical trial evidence supports that either rubber cup or tooth brush prophylaxis will be effective. The preponderance of evidence favors application of varnish to dry teeth and post-operative dietary instructions to include a soft diet for 12 hours. Post-operative brushing instructions should be to avoid brushing for 12 hours. This protocol would allow for at least 12 hours of varnish/tooth contact time. A sample of post-operative instructions is included in Figure I.

For younger children (0-36 months), who may be outside a conventional dental office environment, more data are needed. The authors' recommendation is to dry teeth with gauze pads and apply the same post-operative diet and oral hygiene instructions as recommended for children in a dental office environment.

Better Decay Prevention for Your Child

We are pleased to offer a new and improved method of decay prevention to our patients. We are now using a time-released topical fluoride varnish to apply fluoride to children's teeth in our clinic.

- **The varnish is as effective and safe as the fluoride gel we've used for many years.**
- **The application is quicker and easier, and the fluoride varnish does not have the unpleasant gel taste unpopular with some children.**

When your child leaves our clinic, the teeth will be coated with the varnish and will not look bright and shiny as usual after being cleaned and treated with fluoride gel. They will look nice tomorrow when the varnish has had time to have its maximum effect and has worn off.

To retain the varnish on the teeth for as long as possible and to achieve the best decay prevention:

- **Your child should eat a soft, non-abrasive diet for the rest of the day.**
- **Teeth should not be flossed and brushed until tomorrow morning, at which time a regular schedule of careful oral hygiene should be resumed.**

Thank you for trusting us with your child's oral health!

Figure I. This is a sample of post-operative instructions that can be given to parents by office staff following the application of fluoride varnish.

PRODUCT SELECTION

There are at least 12 varnish products on the marketplace currently. It should be noted that to date, all RCTs investigating 5% NaF fluoride varnish have tested the product Duraphat; indeed, Duraphat was the only 5% NaF varnish under study in every clinical trial cited in this paper. More research is needed to determine the efficacy of the various brands of varnish currently on the market. All have been changed in some way to improve color, taste or some other feature of the Duraphat formulation. It is not known how or whether these changes alter efficacy. While other products may have similar components, none of the other 5% NaF varnish products has met the gold standard of RCT study; furthermore, no clinical equivalency data have been reported to suggest that other products are comparable.

UNANSWERED QUESTIONS/DIRECTIONS FOR FUTURE RESEARCH

More data on safety and patient acceptance have been recommended.[18] Relative to periodicity, semi-annual frequency has received nearly all of the attention of RCTs to date. Data to support more frequent applications are beginning to emerge and this arena needs more systematic study.

More data are needed on the efficacy of varnish for children ages 0-3 to gain a better appreciation for its role in the prevention of early childhood caries and its potential impact on white-spot lesions. Because varnish is the first topical agent safe for infants and toddlers, this realm of investigation is broad and is likely to include research environments such as physicians' offices and community/public health clinics.

SUMMARY

This paper expands upon the evidence-based clinical recommendations for professionally applied topical fluoride as recommended by the ADA's Council on Scientific Affairs. Specifically, we have examined the evidence more closely with an eye on offering clinicians specific age-related guidelines for using fluoride varnish for their child patients. For clinicians to maximize the potential for reductions in caries using varnish, we strongly recommend reliance upon those clinical techniques that have been shown to be the most effective: a pre-application rubber cup or tooth brush prophylaxis, the application of varnish to ***dry*** teeth and post-operative instructions to include both no tooth brushing and a soft diet for 12 hours.

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