EVIDENCE-BASED RECOMMENDATIONS FOR THE USE OF PROFESSIONALLY APPLIED TOPICAL FLUORIDES IN ONTARIO'S PUBLIC HEALTH DENTAL PROGRAMS

Updated report by:
RJ Hawkins, D Locker

1999 report by:
JL Leake, PA Main, E Ho

1995 report by:
GL Woodward, DW Lewis

COMMUNITY DENTAL HEALTH SERVICES RESEARCH UNIT

QUALITY ASSURANCE
REPORT NO. 20

2000

TABLE OF CONTENTS

12.0 Tables

13.0 References

Introduction

This report updates reviews undertaken in 1995 and 1999. The new literature retrieved was limited to those topics that were reviewed in 1999. The updated sections are indicated by bold text.

1.0 The context for evidence-based recommendations

Boards of Health in Ontario have a long history of providing dental treatment to children. Clinical and community-based preventive services, such as fluorides and education, have also been added. Program guidelines have been developed to assist clinicians in making decisions on the preventive services offered to schoolchildren. These guidelines and the underlying evidence-based report also assist managers to: i) allocate resources to achieve maximum impact; and ii) to assure the quality of patient care.

2.0 The need to examine professionally applied topical fluorides

Given that topical fluorides are often used in the prevention of dental caries and their application represents a major commitment of staff time, evidence supporting and recommendations to guide their use were examined in 1995 (Woodward & Lewis) and 1999 (Leake et al.). The 1999 report was based on the evidence available before 1997. **Since then, additional clinical studies have been reported in the scientific literature. This report provides an update to the 1999 report.**

The purpose of this review is to summarize the scientific evidence on professionally applied topical fluoride (PATF) and to make recommendations on the appropriate use of PATF for Public

Health Dental Programs in Ontario. **The review began in May 2000 and covers the information available up until that date.**

3.0 Structure of this report

The organization of this review follows the template proposed at the RCDSO/CDHSRU workshop on developing clinical guidelines/standards of practice (Leake et al., 1996).

1. Target population;
2. Clinical problem;
3. Clinical flexibility;
4. Summary of evidence;
5. Comparison of costs;
6. Relative importance of the potential outcomes;
7. Evidence-based recommendations and minority views, and
8. Comments and suggestions for further research

4.0 Target population

4.1 Patient populations included

These guidelines apply to children who receive dental care from public health departments in the province of Ontario.

4.2 Patient populations excluded

These guidelines do not apply to adults or seniors.

5.0 Clinical problem

The question addressed in this review is: what is the appropriate use of PATF in the prevention of dental caries? Specifically the report answers:

i) Which PATF therapies should be used?

Common PATF therapies will be evaluated in terms of the:

- expected benefits;
- potential harmful effects;
- ease of application; and
- expected implementation and operating costs.

ii) What procedure should be followed when using the PATF therapies, namely:

- who should receive PATF?
- how often should a child receive PATF?
- is a professional cleaning needed before PATF?
- should a cleaning be followed by a PATF, even if the child is not at high risk?
- how much fluoride should be applied and what general procedure should be used?
- how long should the fluoride preparation be retained in the mouth?

5.1 Prevalence of dental caries

Caries prevalence among children in western countries fell substantially during the 1970s and 1980s (Tubert-Jeannin et al., 1993; Anderson, 1995). Some epidemiological studies have shown the secular trend in caries prevalence may have flattened out in the primary dentition, while the downward trend has continued among those 12-years and above (Truin et al., 1993; ORCA Saturday Afternoon Symposium, 1996). In the United States, a national survey conducted in 1986-87 reported that 50% of schoolchildren (5-17 years) were caries free, compared to 37% in 1979-80 (Newbrun, 1989; Ripa 1991).

In Ontario, 68% of children aged five years had no history of decay (deft + DMFT = 0) in 1994, compared to 42% in 1972 (Leake & Main, 1995). The percentage of 13-year-olds who were caries-free rose from 8% to 52% between 1972 to 1994. Over the same period, the mean caries scores for five-year-olds and 13-year-olds fell from 2.47 to 1.23 deft and from 5.3 to 1.46 DMFT, respectively.

However, not all children experience the same degree of reduction in caries risk and dental caries remains a significant problem in a small group of high-risk children. In the United States, a survey for the National Preventive Dentistry Demonstration Program found that 20% of children accounted for nearly 60% of the total DMFS score (Bohannan et al., 1985). In Ontario, 52.4% of children born in Canada were caries free, compared with 37.6% of those who were born elsewhere (Leake & Main, 1995).

The decline in the prevalence of dental caries has not been uniform across all tooth surfaces. On a percentage reduction basis, the prevalence of occlusal lesions has declined less than lesions on other tooth surfaces. Hence, they make up a higher proportion of the burden of dental caries.

For example, among 5-to-17-year-olds in the United States, occlusal lesions accounted for 89% of dental caries in 1987, compared to 84% in 1979-80 (Li et al., 1993) and 49% in 1971-73 (Bohannan & Bader, 1984). As seen in Table 1, although the greatest absolute decline in caries risk was observed in pit and fissure surfaces, 55.53 per 1,000 surfaces at risk, the percentage decline compared to other surfaces and teeth was lowest, 31%.

Canadian data are available from a study of 6-to-14-year-olds in British Columbia (Table 2) (Clark et al., 1995). Pit and fissure caries accounted for 77% and 74% of all caries lesions in children with and without a lifelong fluoridation history, respectively.

The high prevalence of pit and fissure caries may have important implications for the overall effectiveness of PATF. In terms of the relative reduction in DMFS, PATF is more effective against smooth surface caries than against pit and fissure caries (Woodward & Lewis, 1995). Given the prominence of pit and fissure caries, the absolute effectiveness of PATF needs to be carefully examined.

6.0 Clinical flexibility

These guidelines do not apply to children who are unable to tolerate the procedure because of gag-reflex or medical problems. The guidelines may apply to children who are believed to be at much higher risk of caries due to a physical or other disability. These guidelines do not address the prevention and management of early enamel caries through other technologies (e.g., diet counselling) nor the management of the later stages of the disease when a restoration would ordinarily be required. Individuals may refuse to receive PATF as recommended under these guidelines.

7.0 Evidence for efficacy of PATF

7.1 Search strategy for the update

The search for scientific evidence involved a three-stage process. First, computerized literature searches were conducted on Medline <1997 to May 2000> with the following search strategies:

1. **Textword = topical fluorides**

   or textword = topical fluoride

   or textword = professionally applied fluorides

   or textword = professionally applied fluoride

   Yield = 44 articles

2. **Subject heading = topical fluorides**

   Yield = 143 articles

3. **The two sets of references 1 & 2 were combined.**

   Yield = 156 articles

At the second stage, the authors screened the abstracts of the 156 articles to identify those that might yield scientific evidence relevant to the research questions. Thirty articles were selected. Of these, 25 were available from the libraries at the Faculty of Dentistry, University of Toronto. Five articles were not retrieved because they were published in non-English language journals.

7.2 Inclusion/Exclusion criteria

At the first stage, only those papers involving human subjects and written in English were selected. At the second and third stages studies were ranked according to the level of evidence and the five-category classification of recommendation system developed by the Canadian Task Force on the Periodic Health Examination (CTFPHE) (1994). Papers were selected which had the highest level of evidence available to answer each question. Thus, clinical studies (Levels I and II-1) or review articles based on Levels I or II-1 evidence were included. For the current review, only seven of the 25 selected articles provided Level I or II-1 evidence (one meta-analysis and six clinical trials). In situations, where clinical studies were unavailable, uncontrolled studies or expert opinion were used (Levels II-2 to III). For this review, three reviews of fluoride varnish were included.

The CTFPHE system of ranking the quality of evidence applies to studies assessing causation or the efficacy of an intervention. It does not apply to studies assessing a diagnostic or predictive test, the prognosis of disease, or the economic evaluation of two effectiveness interventions. However, quality appraisal criteria for such studies do exist (Leake, 1997) and were employed to classify recommendations based on other study designs.

7.3 Alternative forms of PATF

Previous reports identified three fluoride compounds: 2% sodium fluoride, 8% stannous fluoride, and 1.2% acidulated phosphate fluoride (APF); and three vehicles used to apply these fluorides: brush-on solutions, gels applied in trays, and varnishes. The 1995 report also cited the popularity of APF among dentists and the relative ease of application of gels. The 1995 report

recommended the use of APF gel. Since 1992 there has been mounting documentation of the efficacy of fluoride varnishes in preventing caries. **Therefore, consistent with the 1999 report, this report also examines whether fluoride varnish should be recommended over APF gel.**

7.4 Evidence of the caries preventive effects of APF gels and fluoride varnishes

1995 Report

The 1995 report did not identify any clinical study examining or comparing the anti-caries effect of APF gel and fluoride varnish. At the time of that review, experts believed that there was no difference in their effectiveness (Ripa, 1990).

7.4.1 Efficacy of APF gel

1999 Report

One randomized controlled trial of APF gel was conducted in two non-fluoridated areas in Quebec (Olivier et al., 1992). Biannual applications of 1.2% APF gel on children at medium-to-high risk (3-to-14 defs at age 6) showed a statistically significant reduction in caries increments over two years of 0.92 surfaces or 34.3% (Table 3). However, after stratification by tooth surfaces, only the reduction in occlusal caries was significant (0.53 surfaces or 33.8%, over the study period). This points out an often overlooked finding - that if the absolute number of surfaces saved from decay is used as the measure of effectiveness, rather than the relative reduction, topical fluorides are more effective in preventing pit and fissure caries than they are in preventing smooth surface decay.

2000 Update

No recent clinical trials using APF gel, applied with trays, were found. One study was found in which other gel types, NaF and SnF_2, were applied to approximal tooth surfaces by professional flossing (Gisselsson et al., 1999). In this study, 280 13-year-old Swedish schoolchildren were randomly allocated to one of three groups: NaF gel; SnF_2 gel; or placebo gel. Children were treated 4 times a year for 3 years. Treatments required about 10 minutes per visit and were carried out by dental nurses. After 3 years, there was a reduction in mean approximal caries increment, compared to the placebo group, of 39% and 30% in the SnF_2 and NaF groups, respectively. A significant difference ($p < 0.05$) in mean approximal caries increment was found between the placebo and SnF_2 groups, but the difference between test groups was not significant.

A meta-analysis, on the caries-inhibiting effect of fluoride gel treatment in 6-15-year-old children, was performed using published data from 1967 to 1992 (van Rijkom et al., 1998). The overall prevented fraction in fluoride gel treatment studies was 22%, indicating the reduction of caries incidence by fluoride gel treatment relative to the incidence in the control group. However, the application method differed between studies and only 9 of the 19 selected studies used professional methods; the other 10 studies used self-applied methods. Although no separate prevented fraction was given for those studies which used professional application methods, multiple regression analysis showed no significant influence on prevented fractions for the variables 'application method', and 'application frequency'. Regardless, an important drawback to this meta-analysis was that no clinical studies were found which examined low-risk child populations using fluoride toothpaste. Thus, the

currently low levels of caries incidence in developed countries were not reflected in the samples included in the meta-analysis.

7.4.2 Efficacy of Fluoride Varnish

1999 Report

In a meta-analysis on the caries preventive effect of Duraphat™ fluoride varnish, eight studies were identified that were of high quality and provided Level I or Level II evidence (Helfenstein & Steiner, 1994a, 1994b). Applying a random effects model on these studies, it was estimated that, overall, the use of Duraphat™ results in a 38% reduction of caries increment (95% CI = 19-57%). An additional six studies were included in a second analysis, using a specialized statistical procedure (bootstrap estimate of the standard error). In this analysis, the estimated effect was again a 38% reduction. However, the 95% CI was much narrower, 25%-50%. These findings provided Level I evidence of the anti-caries effect of Duraphat™.

2000 Update

Two clinical trials were identified which provided Level I evidence supporting the effectiveness of fluoride varnish for caries prevention (Petersson et al., 1998a; Zimmer et al., 2000). In a two-year study, Petersson et al. (1998a) evaluated the caries inhibitory effects of biannual applications of a fluoride varnish (Fluor Protector™) in preschool children in southwest Sweden. After two years, the incidence of approximal lesions was significantly lower in the test group compared to the control group. Children with a baseline dfs score of ≥5 had a 25% reduction in approximal caries compared to similar children in the control

group.

In a four-year study, Zimmer et al. (2000) examined the use of a fluoride varnish (Duraphat™) in a German community with low socio-economic status and generally high caries levels. Compared to a control group which received no fluoride applications, children who had received at least two fluoride varnish applications per year showed a 37% reduction in mean caries increment for the 4-year study period (0.88 DMFT versus 1.39 DMFT, $p < 0.05$).

The effectiveness of Duraphat™ varnish was further supported in 24- and 48-month comparison studies of fluoride varnish and dental sealants (Bravo et al., 1997a, 1997b). In the 24-month report, compared to the control group, the use of fluoride varnish resulted in a 66% reduction in DMFS on non-fissured surfaces and a 38% reduction on fissured surfaces. However, in both the 24- and 48-month reports, dental sealants were found to have superior performance for the prevention of decay.

A mixture of fluoride and chlorhexidine has been tested in two Swedish studies (Twetman & Petersson, 1997; Petersson et al., 1998b). In the first study, 82 children (11-13-years) with high levels of mutans streptococci were randomized into two groups (chlorhexidine varnish or chlorhexidine-fluoride varnish). Within a 2 week period, each subject received two varnish applications to all posterior interproximal sites. After 3-months, mutans streptococci levels were significantly reduced, compared to baseline, for only the group which received the chlorhexidine-fluoride varnish ($p < 0.05$). Based on these results and related findings, the same researchers conducted a 3-year clinical trial which compared fluoride varnish (Fluor Protector™) and chlorhexidine-fluoride varnish (Cervitec™)

(Petersson et al., 1998b). A total of 219 children were randomized in two groups and treated 2 times a year with varnish applications. Interproximal caries was recorded from bitewing radiographs at baseline and after 3 years. At baseline and follow-up, no significant differences were found between the test and control groups; mean interproximal caries incidence (DFS), including enamel caries, was 3.0 in the fluoride varnish group (control) and 3.8 in the chlorhexidine-varnish group (test group). These results suggested the chlorhexidine-fluoride mixture had no additional preventive effect on interproximal decay compared with fluoride varnish alone.

7.4.3 Direct Comparison of the Effectiveness of APF Gel and Fluoride Varnish

1999 Report

The 1999 report identified one head-on comparison of the caries preventive effectiveness of fluoride varnish and APF gel. Seppa et al. (1995) conducted a 3-year RCT to compare the caries preventive effect of NaF varnish and APF gel on high-risk 12-to-13-year-olds (Table 4). Seppa et al. discussed their findings in light of Kingman's "at least as good" criterion for demonstrating efficacy of a newly introduced product (Kingman, 1992). To claim that fluoride varnish is "at least as good as" APF gel, the upper limit of the 90% confidence interval of the ratio of DMFS increment of the varnish group over that of the gel group has to be less than 110%. For approximal surfaces, the upper limit of the 90% CI was 108% but for all others and for the overall effect the upper limit did not meet the criteria. Thus, APF gel remains the intervention with the higher level of effect.

2000 Update

No clinical trials were identified which directly compared APF gel and fluoride varnish. Given the growing amount of evidence regarding fluoride varnishes, such comparisons are warranted.

7.4.4. Harms - Acute Toxicity and Dental Fluorosis: APF Gel Versus Fluoride Varnish

1995 Report

The 1995 report did not discuss the potential harmful effects of PATF. While acute toxicity can occur with excessive ingestion at any age, dental fluorosis is possible only if the excessive ingestion occurs at a time when the tooth enamel is developing. For the central incisors this is roughly from 20 to from 30 months of age, and later for other teeth (Evans & Stamm, 1991). The effect on the prevalence or severity of fluorosis associated with exposure to two fluoride applications during that period has not been documented.

1999 Report

The 1999 report did not identify any clinical studies on the harmful effects of PATF. However, three review articles were found which addressed this issue (Ripa, 1992; Johnston, 1994; Mandel, 1994). Johnston (1994) reviewed the potential harmful effects of fluoride ingestion from the use of PATF. An application of APF gel (1.2% fluoride) or fluoride varnish (2.3% fluoride) may expose the recipient to as much as 61.5 mg and 11.3 mg of fluoride ions, respectively. It has been shown that, even with suction devices, a considerable amount of fluoride was retained after APF gel-tray treatment (on average 7.7 mg in children, 10.3 mg in adults). Studies on fluoride

varnish applications have reported that 0.7 to 14.5 mg of varnish is used per application. Of this, as much as 75% could be ingested (Johnston, 1992). Thus, Johnston concludes that similar amounts of fluoride are ingested after either gel or varnish treatments. Relating these findings to the established threshold for fluoride nephrotoxicity, 50 umol/l, and to the 'probably toxic dose', 5 mg/kg of body weight, he found that topical fluorides gave cause for concern.

Johnston (1994) also cited two clinical studies on the long-term effect of fluoride ingestion from PATF in his review. One retrospective study identified fluoride gel applications as a risk factor for fluorosis among children in an optimally fluoridated area. The second, more powerful, study found no increased prevalence of dental fluorosis in children aged 14-16, after as many as five annual gel applications since the age of 6 to 7.

Ripa (1992) also discussed the significance of fluoride retention after gel treatments. In particular, he stated that dental fluorosis was evidence of systemic fluoride intake that was too high; and he suggested the ingestion of $\geq$ 10 mg of fluoride would exacerbate this overexposure.

Mandel (1994) suggested fluoride ingestion with varnish was lower than that with gel since he felt less fluoride was applied. This opinion was based on the findings of Ekstrand et al. (1980).

2000 Update

This review did not identify any clinical studies on the harmful effects of PATF. Three reviews of fluoride varnishes were found which addressed this issue (Bawden, 1998; Blinkhorn & Davies, 1998; Beltran-Aguilar et al., 2000).

Blinkhorn and Davies (1998) stated that concerns about fluoride varnish are not justified because varnishes set rapidly after application and adhere to teeth, thereby reducing

the risk of rapid ingestion. Furthermore, the authors reported that because varnishes set rapidly, patients can rinse to remove any varnish on gingiva or mucosa. Lastly, the Ekstrand et al. (1980) study was cited to support the use of varnishes over APF gels: "measurements of fluoride in the blood after topical fluoride treatments with varnish show levels lower than acidulated fluoride gels."

In a review of fluoride varnishes, Beltran-Aguilar et al. (2000) concluded that fluoride varnishes are quick and easy to apply and are less likely to be swallowed by young children. "Fluoride varnishes may be a better alternative to fluoride gels to deliver topical fluoride, especially for young children". The authors also noted that contact allergies had been reported and the use of varnish in patients with ulcerative gingivitis and stomatitis is contraindicated. A possible side effect of varnish use is a short-term burning sensation if the varnish comes into contact with the gingival tissue.

Finally, Bawden (1998) has supported the use of fluoride varnish for infants and young children because of the reduced risk of overingestion of fluoride.

8.0 Comparison of Relative Outcomes and Costs of APF Gel and Varnish

1999 Report

Table 5 compares APF gel and fluoride varnish according to five criteria:

- Devices and clinical procedure;
- Ease of use in clinical setting;
- Cost of implementation;
- Cost per patient;
- Quality of evidence supporting their use.

As evident from Table 5, the cost difference between operating a caries prevention program with APF gel or fluoride varnish may be substantial when the application time estimates are considered. Our own estimates of clinical time for the APF gel (inclusive of admission, treatment, discharge and clean-up) is 20 minutes. This contrasts with Seppa's estimate for application of 6 minutes for the gel and 2 minutes for the varnish. If the ratio of times held, then a varnish application would take about 7 minutes in public dental clinics, a considerable saving. However, Seppa's time estimates are not well supported and further research needs to be done. **Based on the results of this update and the 1995 and 1999 reports, APF gel remains the intervention of choice for the application of PATF. Fluoride varnish may be considered as an alternative to APF gel for certain patients (e.g., young children, and patients with gag-reflex or medical problems). However, the use of fluoride varnish, as compared to the use of APF gel, may compromise caries prevention.**

9.0 APF gel application protocol

While APF gel is the choice for the application of PATF, it would not be cost-effective to apply PATF to all children, especially to those who are not likely to experience new decay. Thus, to ensure that outcomes are maximal for the resources committed, the following questions were studied:

- who can benefit from PATF?
- how often should PATF be provided?
- is cleaning required prior to PATF?
- should cleaning be followed by PATF?
- how much of the fluoride preparation should be used? and
- for how long should the fluoride preparation be retained in the mouth?

9.1 Who can benefit from APF gel?

1995 Report

The 1995 report made reference to three clinical studies which investigated the combined effect of PATF, pit and fissure sealants, and water fluoridation (Szwejda, 1972; Bagramian, 1982; Bohannan et al., 1985). The findings suggested that, for annual PATF applications to those living in an optimally fluoridated community and receiving pit and fissure sealants, the incremental anti-caries protection from PATF was minimal. Therefore, PATF does not make a sufficiently large difference in reducing caries for the average low to moderate caries-risk child living in a fluoridated community.

The 1995 report did not examine clinical studies that evaluated risk markers for caries in children. Instead the authors analyzed 1990 North York data and summarized expert opinion. Past caries experience and pattern were cited predictors of caries risk and pattern. They suggested children with pit and fissure caries would benefit more from occlusal sealants than PATF. The review concluded that: "Children who have experienced limited pit and fissure decay were not necessarily at high risk for smooth surface caries, and should not receive topical fluoride. Use of topical fluoride should be directed toward children with one or more decayed smooth surfaces." Based on this conclusion, the 1995 report recommended that "Children with one or more decayed smooth surfaces should receive PATF."

1999 Report

The 1999 report did not identify any recent studies that would allow the estimate of the effectiveness of PATF in fluoridated areas. Two studies on stannous fluoride solution, conducted

in fluoridated communities in the 1960s, were included to supplement the evidence provided in the 1995 review (Muhler, 1960; Horowitz & Heifetz, 1969). Both studies demonstrated the effectiveness of stannous fluoride; PATF applications resulted in statistically significant reductions in DMFT and DMFS. As would be expected, the prevalence and extent of caries among subjects in these earlier studies were higher than currently experienced in most areas of Ontario. Therefore, while the two studies demonstrated the effectiveness of topical fluoride in fluoridated areas, the size of the effect may not be as large among Ontario children who have lower caries scores.

The 1999 report did not find any controlled studies that identified the patient group that would benefit most from PATF. The findings from the Olivier et al. (1992) study show that PATF brought about a significant anti-caries effect in the moderate to high risk group (i.e., those with an initial mean defs of 3 to 14) (Table 3). The anti-caries effect was lost in the extremely high-risk group (baseline defs of 15+) suggesting that, for extremely high-risk children, PATF is insufficient to produce noticeable caries reduction.

Nonetheless, the 1999 report concluded that to ensure the appropriate use of PATF, children at higher risk of caries have to be identified.

2000 Update

This review did not identify any recent clinical trials that would allow the estimate of the effectiveness of fluoride gel treatment in fluoridated areas. A meta-analysis on the caries-inhibiting effect of fluoride gel treatment in 6-15-year-old children was performed by van Rijkom et al. (1998). 'Number needed to treat' (NNT) was used to estimate the efficiency of fluoride gel treatment and the NNT indicated the number of patients that needed to be

treated to prevent 1 DMFS. In a population with low caries incidence (0.25 DMFS/year), the NNT was 18, but in a population with high caries incidence (1.5 DMFS/year) the NNT was 3. Based on the results of this meta-analysis, it was concluded: "From the standpoint of cost-effectiveness, the additional effect of fluoride gel treatment in current low and even moderate caries incidence child populations must be questioned."

9.2 Identifying High-risk Children

A number of risk markers have been suggested (Ripa, 1992; Johnston, 1994; Lewis et al., 1995; Songpaisan et al., 1995) including:

i. Demographic and socio-economic factors:

- age
- poverty

ii. Environmental factors:

- non-fluoridated community

iii. Caries history/activities

- high defs/DMFS count
- development of new caries lesions on previously sound tooth
- secondary lesions associated with restoration margins

iv. Conditions that increase the risk for caries

- ongoing orthodontic treatment
- compromised salivary flow as a result of radiation therapy, chronic medication and medical conditions
- high counts of micro-organisms

The importance of past caries experience as a risk marker was shown in two observational studies. In a 3-year study, Mattiasson-Robertson and Twetman (1993) found salivary mutans streptococci score and past caries, defined as number of colony forming units per $cm^2 \geq 30$ and DMFS > 4, respectively, were predictive of caries risk. Holt (1995) demonstrated that those who were caries-free at baseline developed fewer lesions during the follow-up period. On the other hand, he found 9-year-olds with a baseline dmfs of 1 to 5 had the same caries increment as those with a baseline dmfs of 6 and above. These findings are parallel to observations made on 1990 North York data which suggested children with a DMF of 1 or more had a higher probability (42%) of having one or more newly decayed teeth than children with a DMF of 0 (24%) (Woodward & Lewis, 1995).

The superiority of past caries experience as a predictor of caries risk was also demonstrated in a discussion paper, unpublished, by Hausen (1996). The powers of six predictors were compared using ROC curves from a cohort of 350 13-year-olds. The six predictors were: baseline DMFS; mutans streptococci score; salivary flow rate; sucrose intake frequency score; brushing frequency score; and social group. The predictive power of baseline DMFS score was clearly the highest. In fact, baseline DMFS was the only measure which predicted better than random guessing; its ROC curve was the only one that differed visually from the 'no information' line.

According to conventional practice and as noted above, PATF is an appropriate anti-caries measure for children at medium-to-high risk for both smooth surface and pit and fissure caries. Past caries has also been shown to be a reliable risk marker for overall risk of caries.

For children at risk for pit and fissure caries only, sealants would be the treatment of choice given their higher rates of effectiveness over the longer term. However, there are instances where

the procedure, though indicated, cannot be performed. Parent refusal, lack of compliance from the patient, and partially erupted teeth may preclude dental sealants as a preventive measure. Since there is level I evidence to support that PATF is effective against pit and fissure caries (Olivier, 1992), PATF may be recommended in these cases.

Recommendation

Children with one or more decayed surfaces should receive PATF, and especially those whose permanent molars should, but cannot, be sealed (Level of Evidence: I; Classification of recommendation: B).

9.3 How Often Should APF Gel Be Applied?

1995 Report

The 1995 report identified one completed clinical study that compared the anti-caries effect of annual versus biannual applications of PATF with APF solution (Horowitz & Doyle, 1971). The report also included interim results of a 3-year study conducted by Lewis. The findings suggested there was no greater anti-caries effect when topical fluoride was applied biannually instead of annually. The authors of the 1995 review concluded that:

> "No scientific evidence exists to support the belief that biannual applications of topical APF gel result in greater caries reduction than annual applications."

Based on this conclusion, the authors recommended that:

> "Children with one or more decayed smooth surfaces should receive annual topical fluoride treatments in the year of diagnosis and the following year."

1999 Report

For the 1999 report, the published results of a 3-year randomized community-based clinical trial were available (Johnston & Lewis, 1995). The study compared the anti-caries effect of APF gel applications (annual versus biannual), and prior cleaning versus no prior cleaning (Tables 6 and 7). Although the results of this study showed no statistically significant difference in caries increment between annual and biannual applications, it is worth noting that across all four groups there was a trend for biannual applications to produce greater caries reduction: a 1.6% to 22% difference.

Thus, two randomized trials have found no difference between annual and biannual frequencies of application. However, the studies could not control for the number of additional PATF applications received from private dentists. Thus, some children may have received 3 or 4 applications per year. Due to this possibility, an external review committee felt there was insufficient evidence to recommend only one application per year, and recommended the traditional twice-yearly applications be re-instituted.

The 1999 report concluded:

> "Two studies have shown that biannual APF gel applications are no more effective than annual applications of APF gel (Level of evidence: I). However, study subjects may have received additional APF applications outside the study and, therefore, there is insufficient evidence that annual applications are effective."

2000 Update

No recent clinical studies were found which addressed this question. A meta-analysis of 19 studies on the caries-inhibiting effect of fluoride gel treatment found the variable 'application frequency' had no significant influence on fluoride gel effectiveness (van Rijkom et al., 1998). However, the authors suggested this finding may be due to the small number of professional tray-application studies which were included in the analysis. In addition, all studies using an annual gel application were from the early 1970s, whereas studies using biannual gel applications were published in the late 1970s or early 1980s. No studies were included which compared annual versus biannual application frequencies.

Recommendation

Consistent with the 1999 report, APF gel should be provided on a biannual basis (Level of evidence: I; Classification of recommendation: A).

9.4 Is Cleaning Required Prior to APF Gel Applications?

1995 Report

The 1995 report identified three randomized clinical studies that investigated the need for a cleaning prior to PATF. All three studies found there was no difference in the anti-caries effect of PATF with and without prior cleaning. It was therefore concluded: "A prophylaxis is not necessary before a topical fluoride application." Based on this conclusion, it was recommended: "No prophylaxis is necessary before the application of topical fluoride."

1999 Report

The 1999 report again cited the Johnston and Lewis' study (1995) which also examined the anti-caries effect of APF gel with and without prior cleaning. The comparison of defs/DMFS or DMFS increments across the four groups showed no apparent advantage or disadvantage of a cleaning before gel applications (Tables 6 and 7). While additional cleaning might also have been provided outside the study, in this case the finding is supported by previous randomized trials where cleaning was tested directly. It was concluded that, for dental caries prevention, cleaning is unnecessary before the application of topical fluoride.

2000 Update

No recent clinical studies were found which addressed this question.

Recommendation

As per the 1995 and 1999 reports, for dental caries prevention, cleaning is unnecessary before the application of topical fluoride (Level of evidence: I; Classification of recommendation: E).

9.5 Should Cleaning be Followed by the APF Gel Application?

1995 Report

The authors noted that the clinical significance of a post-cleaning APF gel application on the risk of decay has never been studied directly. Therefore, the results from two studies which investigated the cariostatic effect of fluoridated versus non-fluoridated prophylaxis pastes were

examined to determine indirectly the impact of a cleaning without a subsequent PATF on a child's susceptibility to tooth decay (Axelsson & Lindhe, 1974, 1975; Lindhe et al., 1975). A fluoridated prophylaxis paste was no more effective in caries prevention than a non-fluoridated paste. Ripa et al. (1976) conducted a two-year study and showed that biannual cleaning had no cariostatic effect. Despite the lack of evidence to suggest a single cleaning increases a child's risk of caries, fluoridated prophylaxis pastes are recommended over non-fluoridated pastes when the procedure is not followed by PATF (AAPD, 1992; Johnston, 1992). The 1995 report concluded that:

> "Prophylaxis and topical fluoride use should be considered independently of one another. There is no evidence to suggest an annual or biannual prophylaxis alone, without a subsequent application of topical fluoride, will increase a child's risk of caries. Therefore, a topical fluoride treatment is not necessary following a prophylaxis."

Hence, it was recommended that:

> "It is not necessary to follow a prophylaxis with a topical fluoride application unless a topical is indicated based on the child's oral health status. If no topical fluoride treatment will follow a prophylaxis, a fluoridated prophylaxis paste is recommended."

1999 Report

The 1999 report acknowledged that rubber-cup prophylaxis (cleaning) is required to remove extrinsic stain from teeth. The review did not identify any additional studies that examined the need to follow a cleaning with PATF. However, Johnston (1994) suggested fluoridated prophylactic paste might be used when no topical fluoride application was to follow the cleaning procedure. Consistent with the 1995 report, professional cleaning and topical fluoride use should

be considered independently of one another. There is good evidence to suggest an annual or biannual cleaning alone, without a subsequent application of topical fluoride, will not increase a child's risk of caries (Ripa et al., 1976). Therefore, a topical fluoride treatment is not necessary following a cleaning (Level of evidence: I).

2000 Update

No recent clinical studies were found which addressed this question.

Recommendations

As per the 1995 and 1999 reports, rubber-cup prophylaxis (cleaning) is required to remove extrinsic stain from teeth. It is not necessary to follow a cleaning with a topical fluoride application unless a topical is indicated based on the child's oral health status (Ripa et al., 1976), (Level of evidence: I; Classification of recommendation: E). If no topical fluoride treatment will follow a cleaning, a fluoridated prophylaxis paste is recommended (AAPD, 1992), (Level of evidence III; Classification of recommendation: C).

9.6 How Much of the APF Gel Should be Used? and

9.7 What General Procedure Should be Followed?

1995 Report

The 1995 report did not include any clinical studies that examine the impact of the amount of gel used on the plasma fluoride concentration and on the anti-caries effect. However, based on the recommendations on the use of PATF from four review articles (Lecompte, 1987; Ripa, 1987,

1991; Johnston, 1992), the following conclusions and recommendations were made. "To reduce fluoride ingestion only enough gel should be applied to cover all teeth, but this should not exceed 2-2.5 grams of gel per tray or over 40% of the tray's volume. Patients should be seated upright, suction should be used during and after the application, and expectoration should occur for at least 30 seconds immediately following the procedure. For young children, the fluoride gel should be wiped off after application."

"APF gel should be used and applied using a styrofoam tray. Enough gel should be used to completely cover the teeth, but this should be no more than 2-2.5 grams per tray or 40% of the tray's volume. Patients should expectorate for at least 30 seconds after the fluoride trays are removed, and gel should be wiped from teeth of young patients. All patients should be instructed not to eat or drink anything for at least 30 minutes."

1999 Report

The 1999 review did not reveal any new clinical trials on this research question. However, the issue had been reviewed again by a number of authors (Ripa, 1992; Johnston, 1994, Lewis et al., 1994; Warren & Chan, 1997). There was consensus on the need to minimize the amount of fluoride ions ingested while maximizing fluoride absorption by enamel. The following steps have been recommended by these authors (Level of evidence: III):

1. Minimize ingestion of fluoride:
   - sit patient upright;
   - use a maximum of 2.5-4 ml per full size trays (less for small trays);

- use tray with absorptive liners;
- use high-speed suction during and after the procedure; and
- ask patients to expectorate for a minute after tray is removed.

2. Maximize absorption of fluoride by enamel:
   - select tray that covers all sites;
   - dry each arch then insert upper tray and lower tray separately;
   - apply saliva absorbers to the parotid duct openings for difficult cases; and
   - ask patients not to rinse, eat or drink for 30 minutes after the procedure.

2000 Update

No recent clinical studies were found which addressed this question.

Recommendation

Enough gel should be used to completely cover the teeth, but this should be no more than 2-2.5 grams per tray or 40% of the tray's volume. Teeth should be air-dried before gel application. Patients should be seated upright and suction should be used during the procedure. After the procedure, patients should be instructed to expectorate for at least 30 seconds, and gel should be wiped from teeth of young patients. All patients should be instructed not to eat or drink anything for at least 30 minutes (Level of evidence: III; Classification of recommendation: C).

9.8 For How Long Should the APF Gel be Retained in the Mouth?

1995 Report

The authors could not locate any clinical trials comparing the cariostatic effectiveness of 1-minute versus 4-minute application of APF gel. Fluoride uptake was shown to be significantly greater after 4 minutes than one minute by one in vitro and one in vivo experiment (Wei & Hattab, 1988; Wei et al., 1988). These findings supported expert recommendations on the adoption of a 4-minute application time. Based on these findings, the following conclusions and recommendations were made: "Topical fluoride application time should be 4 minutes, not 1 minute"; and "...Gel should be retained on the teeth for 4 minutes...".

1999 Report

The 1999 review did not identify any clinical studies on the relationship between exposure time and effectiveness of PATF. Two *in vitro* experiments were published, but they had conflicting findings. Garcia-Godoy et al. (1995) found lesions artificially created after a 1-minute versus a 4-minute APF gel exposure were not significantly different in size. However, using 2% NaF solutions at Ph 3.5 and 5.5, Cruz and Rolla (1992) showed the amount of calcium fluoride deposited increased rapidly with time of exposure. The validity of the findings from these two studies is questionable due to the limited power of each study; sample size ≤ 10 in each treatment group. The statistical tests used were not appropriate for the study design, further undermining the findings.

A number of review articles have been published (Ripa, 1992; Wei & Yiu, 1993; Johnston, 1994). There was consensus among these authors on the use of a 4-minute exposure to optimize

the benefit of APF gel. The recommendation of the 1995 report was upheld.

2000 Update

This review did not identify any clinical studies on the relationship between exposure time and effectiveness of PATF.

Recommendation

As per the 1995 and 1999 reports, topical fluoride application time should be 4 minutes, not 1 minute (Ripa, 1992; Wei & Yiu, 1993; Johnston, 1994), (Level of evidence: III; Classification of recommendation: C).

10.0 Summary of Evidence-based recommendations

APF Gel and Fluoride Varnish

Both APF gel (Olivier et al., 1992) and fluoride varnish (Helfenstein & Steiner, 1994a, 1994b) are efficacious and can be recommended (Level of evidence: I; Classification of recommendation: A).

Fluoride varnish, while efficacious, has not been found to be superior to or "at least as good as" APF gel (Seppa et al., 1995). However, there may be a significant cost advantage in favour of fluoride varnish but it is poorly documented. Thus, APF gel remains the first choice for PATF (Level of evidence: I; Classification of recommendation: B).

Application Procedure of APF Gel

The 1999 report identified scientific evidence that supported the recommendations made in the 1995 report regarding the application procedure of APF gel. Based on additional evidence published after 1995, the recommendations made in relation to the question who should receive APF gel application? and what general procedure should be followed, were expanded. All recommendations are listed below:

Who should receive PATF?

- Children with one or more decayed surfaces should receive PATF and especially those whose permanent molars should, but cannot, be sealed (Level of evidence: I; Classification of recommendation: B).

How often should PATF be provided?

- APF gel should be provided on a biannual basis to those meeting the above criterion (Level of evidence: I; Classification of recommendation: A).

Is cleaning required prior to PATF?

- No cleaning is necessary before the application of topical fluoride (Level of evidence: I; Classification of recommendation: E).

Should cleaning be followed by PATF?

• It is not necessary to follow a cleaning with a PATF unless a topical fluoride is indicated based on the child's oral health status (Level of evidence: I; Classification of recommendation: E). If no topical fluoride treatment will follow a cleaning, fluoridated prophylaxis paste is recommended for the cleaning (Level of evidence: III; Classification of recommendation: C).

How much of the fluoride preparation should be used and what general procedure should be followed?

• Enough gel should be used to completely cover the teeth, but this should be no more than 2-2.5 grams per tray or 40% of the tray's volume. Teeth should be air-dried before gel application. The patient should be seated upright and suction should be used during the procedure. After the procedure, the patient should be instructed to expectorate for at least 30 seconds, and gel should be wiped from teeth of young patients. All patients should be instructed not to eat or drink anything for at least 30 minutes (Level of evidence: III; Classification of recommendation: C).

For how long should the fluoride preparation be retained in the mouth?

• APF gel should be retained in the mouth for 4 minutes (Level of evidence: III; Classification of recommendation: C).

11.0 Comments and further research

APF gel remains the preferred form of PATF when considering caries prevention efficacy. Although a growing amount of evidence indicates that fluoride varnish is efficacious in caries prevention and may reduce fluoride ingestion as compared to APF gel, the studies identified lack the power to demonstrate the clinical superiority of fluoride varnish over APF gel. Further studies are needed to compare the amounts used per patient, the relative costs, and patient acceptability of the application of varnishes.

Further research is also recommended on the relative effects of annual and bi-annual treatments and the use of fluoridated versus non-fluoridated prophylaxis pastes.

12.0 Tables

Table 1. Tooth surfaces attacked per thousand surfaces at risk in permanent teeth by type of surface in US children in 1980 and 1987

Type of surfaces	1980	1987	Difference	Percent Reduction
Pit & fissure of molars & premolars (including buccal pits & lingual grooves)	191.46 (84%)	135.93 (89%)	55.53	31.03
Approximal surfaces of molars & premolars	27.31 (12%)	13.40 (9%)	13.90	51.86
All other surfaces	8.21 (4%)	3.71 (2%)	4.50	59.10

Source: Li et al., 1993

Table 2. Mean DMFS by fluoride history and tooth surface

Fluoridation	Total	Occlusal pit/fissure	Buccal/Lingual pit/fissure
Lifelong history	1.66	0.75 (45%)	0.53 (32%)
No history	2.52	1.13 (45%)	0.74 (29%)

Source: Clark et al., 1995

Table 3. Two-year mean DMFS increments for Quebec test and control groups

Stratum (Baseline defs)	Incidence of caries									
	Test group				Control group				Difference	
	Total	Occ.	B-L	M-D	Total	Occ.	B-L	M-D	Abs.	%
All	2.94				3.24				0.30	9.3
3 to 14	1.76				2.68				0.92*	34.3
		1.04				1.57			0.53*	33.8
			0.63				0.99		0.36	36.4
				0.09				0.12	0.03	25.0
≥15	3.45				3.52				0.07	2.0

Source: Olivier et al., 1992

Note: Occ. = occlusal surfaces; B-L = bucco-lingual surfaces; M-D = proximal surfaces; Abs. = Absolute difference; % = Percent difference

* p-value ≤ 0.05

Table 4. DMFS increments for the APF gel and fluoride varnish subjects

Surfaces	Ratio (DMFS increment for varnish/DMFS increment for gel)	Difference (DMFS increment for gel - DMFS increment for varnish)	
		Absolute	Percentage
All	0.88	0.45	12%
Occlusal	1.07	---	-7%
Bucco-lingual	0.85	---	15%
Approximal	0.76	---	24%

Source: Seppa et al., 1995

Table 5. Comparison of costs of providing APF gel and fluoride varnish

	APF Gel	Fluoride varnish
Device & clinical procedure	Acidulated phosphate fluoride (1.23% fluoride); applied using styrofoam trays	Sodium fluoride (2.26% fluoride); applied using a small brush or cotton swab
Ease of use	Easy	Easy
Costs:		
Implementation	Negligible	Negligible
Material	Minimal	Minimal
Application (time)	2 X 20 minutes annually * 2 X 6 minutes annually **	2 X 2 minutes annually **
Quality of evidence	Level I, Class A	Level I, Class A

* Source: Woodward et al., 1994
** Source: Seppa et al., 1995

Table 6. Treatment of the four test groups

Prior Cleaning	Application Frequency	
	Annual	Biannual
No	- annual fluoride gel tray application	- biannual fluoride gel tray application
Yes	- rubber cup cleaning using a non-fluoride prophylaxis paste - annual fluoride gel tray application	- rubber cup cleaning using a non-fluoride prophylaxis paste - biannual fluoride gel tray application

Source: Johnston & Lewis, 1995

Note: All fluoride applications were provided by one of two hygienists or one preventive dental assistant using the manufacturer's recommended methods.

Table 7. Caries increments by frequency of application (dmfs/DMFS for 6-7 year-olds and DMFS for 10-11 year-olds)

	Frequency of application		Difference (annual - biannual)	
	Annual	Biannual	Absolute	Percentage (%)
6-7 year-olds without cleaning	3.82	3.53	0.29	7.6
6-7 year-olds with cleaning	5.04	3.93	1.11	22.0
10-11 year-olds without cleaning	2.54	2.50	0.04	1.6
10-11 year-olds with cleaning	2.46	2.22	0.24	9.8

Source: Johnston & Lewis, 1995

13.0 References

American Academy of Paediatric Dentistry. Reference Manual 1991-1992. Strategic Planning Document, Dental Health Objectives for the Year 2000, Constitution & Bylaws, Oral Health Policies, Guidelines, and Quality Assurance Criteria for Paediatric Dentistry. Chicago, IL, 1992.

Anderson RJ. Changes in dental caries experience of 12-year-old school children in two Somerset schools: a review after an interval of 30 years. Br Dent J 1995;179:125-129.

Axelsson P, Lindhe J. The effect of a preventative programme on dental plaque, gingivitis, and caries in schoolchildren. Results after one and two years. J Clin Periodontol 1974;1:126-128.

Axelsson P, Lindhe J. Effect of fluoride on gingivitis and dental caries in a preventative program based on plaque control. Community Dent Oral Epidemiol 1975;3:156-160.

Bagramian RA. A 5-year school-based comprehensive preventive program in Michigan, U.S.A. Community Dent Oral Epidemiol 1982;10:234-237.

Bawden JW. Fluoride varnish: a useful new tool for public health dentistry. J Public Health Dent 1998;58:266-269.

Beltran-Aguilar ED, Goldstein JW, Lockwood SA. Fluoride varnishes: a review of their clinical use, cariostatic mechanism, efficacy, and safety. J Am Dent Assoc 2000;131:589-596.

Blinkhorn A, Davies R. Using fluoride varnish in the practice. Br Dent J 1998;185:280-281.

Bohannan HM, Bader JD. Future impact of public health and preventive methods on the incidence of dental caries. J Can Dent Assoc 1984;50:229-233.

Bohannan HM, Klein SP, Disney JA, Bell RM, Graves RC, Foch CB. A summary of the results of the National Preventive Dentistry Demonstration Program. J Can Dent Assoc 1985;51:435-441.

Bravo M, Baca P, Llodra JC, Osorio E. A 24-month study comparing sealant and fluoride varnish in caries reduction on different permanent first molar surfaces. J Public Health Dent 1997a;57:184-186.

Bravo M, Garcia-Anllo I, Baca P, Llodra JC. A 48-month survival analysis comparing sealant (Delton) with fluoride varnish (Duraphat) in 6- to 8-year-old children. Community Dent Oral Epidemiol 1997b;25:247-250.

Canadian Task Force on the Periodic Health Examination. The Canadian guide to clinical preventive health care. Health Canada, Ottawa, Canada. 1994.

Clark DC, Hann HJ, Williamson MF, Berkowitz J. Effects of lifelong consumption of fluoridated water or use of fluoride supplements on dental caries prevalence. Community Dent Oral Epidemiol 1995;23:20-24.

Cruz R, Rolla G. The effect of time of exposure on fluoride uptake by human enamel from acidulated fluoride solutions in vitro. Acta Odontol Scand 1992;50:51-56.

Ekstrand J, Koch G, Petersson LG. Plasma fluoride concentration and urinary fluoride excretion in children following application of the fluoride-containing varnish Duraphat. Caries Res 1980;14:185-189.

Evans WR, Stamm JW. An epidemiological estimate of the critical period during which human maxillary incisors are most susceptible to fluorosis. J Public Health Dent 1991;51:251-259.

Garcia-Godoy F, Hicks MJ, Flaitz CM, Berg JH. Acidulated phosphate fluoride treatment and formation of caries-like lesions in enamel: effect of application time. J Clin Pediatr Dent 1995;19:105-110.

Gisselsson H, Birkhed D, Emilson CG. Effect of professional flossing with NaF or SnF_2 gel on approximal caries in 13-16-year-old schoolchildren. Acta Odontol Scand 1999;57:121-125.

Hausen H. Caries prediction (unpublished). Institute of Dentistry, University of Oulu, Finland. 1996.

Helfenstein U, Steiner M. Fluoride varnishes (Duraphat): a meta-analysis. Community Dent Oral Epidemiol 1994a;22:1-5.

Helfenstein U, Steiner M. A note concerning the caries preventive effect of Duraphat. Community Dent Oral Epidemiol 1994b;22:6-7.

Holt RD. The pattern of caries in a group of 5-year-old children and in the same cohort at 9 years of age. Community Dent Health 1995;12:93-99.

Horowitz HS, Doyle J. The effect on dental caries of topically applied acidulated phosphate fluoride: results after three years. J Am Dent Assoc 1971;82:359-365.

Horowitz HS, Heifetz SB. Evaluation of topical applications of stannous fluoride to teeth of children born and reared in a fluoridated community: final report. J Dent Child 1969;36:65-71.

Johnston DW. The current status of professionally applied topical fluorides. A paper from the workshop "Evaluation of Current Recommendations Concerning Fluorides," Toronto, Canada. 1992.

Johnston DW. Current status of professionally applied topical fluorides. Community Dent Oral Epidemiol 1994;22:159-163.

Johnston DW, Lewis DW. Three-year randomized trial of professionally applied topical fluoride gel comparing annual and biannual applications with/without prior prophylaxis. Caries Res 1995;29:331-336.

Kingman A. Statistical vs clinical significance in product testing: can they be designed to satisfy equivalence? J Public Health Dent 1992;52:353-360.

Leake JL, Main PA. Preliminary findings from the 1994 Ontario Children's Dental Health Survey. Can J Community Dent 1995;10:38-43.

Leake JL, Main PA, Ho E. Evidence-based recommendations for the use of professionally applied topical fluorides in the North York Public Dental Program: an evidence-based report. Quality Assurance Report No. 19, Community Dental Health Services Research Unit, Updated 1999.

Leake JL, Main PA, Woodward GL. Report on the RCDSO/CDHSRU Workshop on Developing Clinical Guidelines/Standards of Practice. Quality Assurance Report No. 15, Community Dental Health Services Research Unit, 1996.

Leake JL. Checklists for appraising evidence in health care. Toronto, Canada. Faculty of Dentistry, University of Toronto Clinical Epidemiology Course Package (DEN1040H) 1997.

Lecompte EJ. Clinical application of topical fluoride products - risks, benefits, and recommendations. J Dent Res 1987;66:1066-1071.

Lewis DW, Ismail AI, and the Canadian Task Force on the Periodic Health Examination. Periodic health examination, 1995 update: 2. Prevention of dental caries. Can Med Assoc J 1995;152:836-846.

Li SH, Kingman A, Forthofer R, Swango P. Comparison of tooth surface-specific dental caries attack patterns in US schoolchildren from two national surveys. J Dent Res 1993;72:1398-1405.

Lindhe J, Axelsson P, Tollskog G. Effect of proper oral hygiene on gingivitis and dental caries in Swedish schoolchildren. Community Dent Oral Epidemiol 1975;3:150-155.

Mandel ID. Fluoride varnishes - a welcome addition (Guest editorial). J Public Health Dent 1994;54:67.

Mattiasson-Robertson A, Twetman S. Prediction of caries incidence in schoolchildren living in a high and a low fluoride area. Community Dent Oral Epidemiol 1993;21:365-369.

Muhler JC. The anticariogenic effectiveness of a single application of stannous fluoride in children residing in an optimal communal fluoride area. II. Results at the end of 30 months. J Am Dent Assoc 1960;61:431-438.

Newburn E. Effectiveness of water fluoridation. J Public Health Dent 1989;49:279-289.

ORCA Saturday Afternoon Symposium 1995. The prevalence of dental caries in Europe 1990-1995. Caries Res 1996;30:237-255.

Olivier M, Brodeur JM, Simard PL. Efficacy of APF treatments without prior toothcleaning targeted to high-risk children. Community Dent Oral Epidemiol 1992;20:38-42.

Petersson LG, Twetman S, Pakhomov GN. The efficiency of semiannual silane fluoride varnish applications: a two-year clinical study in preschool children. J Public Health Dent 1998a;58:57-60.

Petersson LG, Magnusson K, Andersson H, Deierborg G, Twetman S. Effect of semi-annual applications of a chlorhexidine/fluoride varnish mixture on approximal caries incidence in schoolchildren: a three-year radiographic study. Eur J Oral Sci 1998b;106:623-627.

Ripa LW, Barenie JT, Leske GS. The effect of professionally administered biannual prophylaxes on the oral hygiene, gingival health, and caries score of schoolchildren. J Preven Dent 1976;3:22-26.

Ripa LW. Topical fluorides: a discussion of risks and benefits. J Dent Res 1987;66:1079-1083.

Ripa LW. An evaluation of the use of professional (operator-applied) topical fluorides. J Dent Res 1990;69(Spec Iss):786-796.

Ripa LW. A critique of topical fluoride methods (dentifrices, mouthrinses, operator- and self-applied gels) in an era of decreased caries and increased fluorosis prevalence. J Public Health Dent 1991;51:23-41.

Ripa LW. Office fluoride gel-tray treatments current recommendations. New York State Dent J 1992;February:48-50.

Seppa L, Leppanen T, Hausen H. Fluoride varnish versus acidulated phosphate fluoride gel: a 3-year clinical trial. Caries Res 1995;29:327-330.

Songpaisan Y, Bratthall D, Phantumvanit P, Somridhivej Y. Effects of glass ionomer cement, resin-based pit and fissure sealant and HF applications on occlusal caries in a developing country field trial. Community Dent Oral Epidemiol 1995;23:25-29.

Szwejda LF. Fluorides in community programs: a study of four years of various fluorides applied topically to the teeth of children in fluoridated communities. J Public Health Dent 1972;32:25-33.

Truin GJ, van't Hof MA, Kalsbeek H, Frencken JE, Konig KG. Secular trends of caries prevalence in 6- and 12-year-old Dutch children. Community Dent Oral Epidemiol 1993;21:249-252.

Tubert-Jeannin S, Albuisson E, Planche R. Changes in oral health conditions among 6-to-15-year-old children in Auvergne (France) 1987-1991. Community Dent Health 1993;10:251-258.

Twetman S, Petersson LG. Efficacy of a chlorhexidine and a chlorhexidine-fluoride varnish mixture to decrease interdental levels of mutans streptococci. Caries Res 1997;31:361-365.

van Rijkom HM, Truin GJ, van't Hof MA. A meta-analysis of clinical studies on the caries-inhibiting effect of fluoride gel treatment. Caries Res 1998;32:83-92.

Warren DP, Chan JT. Topical fluorides: efficacy, administration, and safety. Gen Dent 1997;45:134-142.

Wei SHY, Hattab FN. Time dependence of enamel fluoride acquisition from APF gels. I. In vitro study. Paediatr Dent 1988;10:168-172.

Wei SHY, Lau EWS, Hattab FN. Time dependence of enamel fluoride acquisition from APF gels. II. In vivo study. Paediatr Dent 1988;10:173-177.

Wei SHY, Yiu CKY. Evaluation of the use of topical fluoride gel. Caries Res 1993;27 (suppl 1):29-34.

Woodward GL, Csima A, Leake JL, Ryding WH, Main PA. Time required by North York dental teams to carry out various dental procedures. Quality Assurance Report No. 7, Community Dental Health Services Research Unit, 1994.

Woodward GL, Lewis DW. The use of professionally applied topical fluorides in the North York Public Dental Program. Quality Assurance Report No. 8, Community Dental Health Services Research Unit, 1995.

Zimmer S, Robke FJ, Roulet J-F. Caries prediction with fluoride varnish in a socially deprived community. Community Dent Oral Epidemiol 2000;27:103-108.