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ABSTRACT

The caries-preventive benefits of fluoride are generally accepted by dental researchers and practicing professionals worldwide. The benefits of fluoride toothpastes and mouthrinses have been supported by several high-quality systematic reviews. The formulation of a fluoride toothpaste and biological (salivary flow rate) and behavioral factors (brushing frequency, brushing time, post-brushing rinsing practices, timing of brushing, and amount of toothpaste applied) can influence anticaries efficacy. Fluoride mouthrinses have simpler formulations and can have better oral fluoride retention profiles than fluoride toothpastes, depending on post-brushing rinsing behaviors. Fluoride continues to be the mainstay of caries control; however, there is still the need to determine the most effective approach for fluoride utilization in children and adults who remain caries-active.

Fluoride toothpastes are the most widely used form of fluoride delivery and have been shown to be effective anticaries agents based on several systematic quantitative evaluations, including a Cochrane review (Marinho *et al*., 2003a) and a Swedish Council on Technology Assessment in Health Care review (Twetman *et al*., 2003), which provide the highest standard of evidence. Marinho *et al*. (2003a), in a meta-analysis of 70 trials on the effectiveness of fluoride toothpaste for the prevention of dental caries in children compared with placebo, found evidence that the use of fluoride toothpastes has a caries-inhibiting effect [average reduction in DMFS of 24% (95% CI, 21% to 28%)] on the permanent dentition; however, there was little information on the effect of fluoride toothpaste on caries incidence in the deciduous dentition.

Our mechanistic understanding regarding how fluoride toothpaste works and how its benefits can be optimized comes from many sources – *in vitro*, *in situ,* and clinical studies involving fluoride kinetics in oral fluids. At a rudimentary level, the efficacy of fluoride is determined by the toothpaste formulation and the toothbrushing behavioral and biological factors (Zero, 2006). Ideally, toothpaste should be formulated to deliver fluoride to the oral cavity in an ionic form (for sodium fluoride and stannous fluoride, F^-; for monofluorophosphate, $PO_3F^{=}$ and F^- combined) available to interact with the dental hard tissues and biofilm during toothbrushing (application phase) and during the time period that fluoride remains in the oral cavity before being cleared to below-effective levels (retention phase; Zero *et al*., 1988). This can be considered as the bioavailable fluoride, which is much more important than the fluoride concentration on the toothpaste label. A study of marketed toothpastes from developing countries around the world found that there were deficiencies in the total and free ionizable fluoride concentrations in a random selection of 101 toothpastes (van Loveren *et al*., 2005). The solubility of the fluoride compound, the abrasive system, and other excipients commonly found in toothpaste can limit fluoride's bioavailability and thus clinical efficacy. Almost all of the current clinical evidence on the effectiveness of fluoride toothpaste is based on studies conducted many decades ago (Zero, 2006) with toothpastes having relatively simple formulations compared with the modern multifunction toothpastes currently marketed (Stamm, 2007). An additional concern is that toothpaste fluoride bioavailability can be reduced as products age, and clinical trials are generally conducted with freshly manufactured toothpaste and do not account for the effects of shelf-life.

Fluoride mouthrinses are recommended as an adjunct to fluoride toothpaste for individuals who are at higher risk of developing dental caries. Marinho *et al*. (2003b) reported that the supervised use of fluoride mouthrinse by children is associated with a clear reduction [average preventive fraction of 26% (95% CI, 23% to 30%)] in caries increment, based on a meta-analysis of 34 trials. The Cochrane review compiling the evidence on all main topical fluoride treatments (Marinho *et al*., 2003c) has concluded that fluoride mouthrinse can also reduce dental caries regardless of exposure to water fluoridation. Based on 8 trials (from the 1970s and 1980s), Twetman *et al*. (2004) found a preventive fraction of 29% for daily and weekly rinses in the permanent teeth of schoolchildren and adolescents with no additional fluoride exposure; however, they questioned if there was additional anticaries benefit of fluoride mouthrinses in children who regularly use fluoride toothpaste. Fluoride mouthrinses have a much simpler formulation than toothpastes and generally do not have fluoride bioavailability problems if properly manufactured. Mechanistically, fluoride mouthrinses can have better oral

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Key Words

caries, fluoride(s), dentifrice(s), mouthrinse(s), toothbrushing, prevention.

Table. Proposed Best Practices for Self-applied Fluoride Administration

Self-applied Fluoride	Strategies	Best Practice
F toothpaste	F concentration	1000 - 1500 ppm F (minimum 800 ppm bioavailable F)
	Brushing frequency	At least twice *per* day
	Starting age	Supervised brushing when teeth first erupt
	Amount of F toothpaste	6 mos - 2 yrs: thin smear, half a pea (0.05 - 0.1 g) 2 - 6 yrs: pea size or width of toothbrush (0.25 g) 6 and older: full length of toothbrush (1 - 1.5 g)
	Brushing time	Minimum 2 mins with a technique that encourages the dispersion of toothpaste around the teeth
	Supervision	Assisted/supervised brushing up to age 8
	Post-brushing behaviors	Spit out the toothpaste and minimize rinsing behaviors with water
	Timing	Ideally, after meals, in the morning, and immediately before bed (other times may also be appropriate, *i.e.*, after lunch in school-based brushing programs)
	Affordability/public acceptance	Needs to be considered as an essential public health measure and not subject to taxation
	Promotion	Encourage oral care companies to adopt these guidelines in their advertising
	Aging populations	Regular use of higher fluoride-concentration toothpastes (>1500 ppm F) may be indicated
	Toothpaste flavor	Should be acceptable to children but not encourage swallowing
	Use in areas with different background F levels	Safe to use regardless of low, normal, or high fluoride exposure from other sources, if used as recommended
F mouthrinse	F concentration and frequency	Daily rinsing (0.05% NaF) or in once-a-week/once-every-two-weeks rinsing programs (0.2% NaF)
	Rinsing time	Ideally, 1 min
	Formulation	Suitable for the age of the individual
	Starting age	Starting at age 4 - 6 yrs, depending on the level of supervision
	Timing of use	Either following fluoride toothpaste use or independent of brushing
	Supervision	Assisted/supervised rinsing up to age 8 yrs

fluoride retention profiles than fluoride toothpaste (Zero *et al*., 1988, 1992b), and, depending on post-brushing rinsing behaviors, individuals who normally rinse with tap water after brushing with fluoride toothpaste may receive an additional benefit from the appropriate use of fluoride mouthrinse (Duckworth *et al*., 2009; Mystikos *et al*., 2011).

This article provides the scientific rationale for the Self-administration Working Group Report developed at the Workshop on the "Effective Use of Fluoride in Asia" held in Phang-Nga, Thailand, March 22-24, 2011. A summary of the proposed best practices for self-applied fluoride administration is given in the Table. The working group consisted of representatives from 20 countries throughout Asia who participated in the development of the guidelines (Siriphant and Srisawasdi, 2011). The content of the working group report is provided in *italics* and the scientific rationale in regular font.

SELF-ADMINISTRATION WORKING GROUP REPORT

Best Practices for Self-applied Fluoride

Fluoride Toothpaste [concentration: range, 1000-1500 ppm fluoride (minimum of 800 ppm F bioavailable is recommended)]

The current levels of fluoride toothpaste products that are marketed worldwide generally fall in the range between 1000 and 1500 ppm F. Walsh *et al*. (2010) reported, based on a network meta-analysis, that the relative caries-preventive effects of fluoride toothpastes increased with higher fluoride concentrations. Based on 74 trials involving D(M)FS scores in the mixed or permanent dentition, the caries-preventive effect of fluoride toothpaste was 23% for 1000/1055/1100/1250 ppm F and 36% for 2400/2500/2800 ppm F; however, toothpastes with 440/500/550 ppm F and below did not show a statistically significant effect compared with placebo. The studies on the deciduous dentition were equivocal.

The concentration in commercially available fluoride toothpaste is based on balancing between delivering a clinically effective level of fluoride and concerns about developing dental fluorosis from fluoride ingestion in children under 6 yrs old (Cochran *et al*., 2004). A clear distinction needs to be made between the fluoride concentration of a toothpaste, which topically interacts with teeth and dental biofilm, and the dose taken up systemically after swallowing and mucosal absorption. Mechanistically, higher fluoride concentrations provide a larger driving force for fluoride to diffuse through plaque and into incipient caries lesions during brushing (application phase) and prolonged retention of fluoride in oral fluids after brushing (retention phase). Higher concentrations are necessary to penetrate caries-prone sites, proximal tooth surfaces, and deep pits and fissures, which are difficult to clean with a toothbrush (Watson *et al*., 2005). Furthermore, higher fluoride concentrations have been shown to prolong retention of fluoride in saliva and plaque (Zero *et al*., 1992b; Nordström and Birkhed, 2009) as

well as in the oral soft tissues, which are also an important fluoride reservoir (Zero *et al*., 1992a).

Brushing Frequency – At least twice per day

Brushing twice *per* day or more has a greater preventive effect than brushing once *per* day (Chestnutt *et al*., 1998; Marinho *et al*., 2003a) and should be recommended for most individuals.

Start Supervised Brushing when Teeth First Erupt

Parents/guardians need to carefully brush their children's teeth when they first erupt into the mouth, both to remove plaque and food debris and to ensure that the teeth are receiving the topical benefits of fluoride at a time when they are most susceptible to caries. The caries susceptibility of enamel is greatest immediately after eruption and tends to decrease with age (Carlos and Gittelsohn, 1965). After they erupt, teeth undergo an adaptation process due to the cycles of intermittent demineralization, caused by biofilm-generated acid from the consumption of fermentable carbohydrates, and remineralization as the biofilm pH returns toward neutrality, rendering them more resistant to subsequent acid challenges (Koulourides *et al*., 1980). The effectiveness of fluoride may be associated with its ability to accelerate the post-eruptive maturation process, and thus, the earlier fluoride comes into contact with teeth, the better.

Amount of F Toothpaste

• from 6 months to 2 years: thin smear, half a pea (0.05 - 0.1 g) on a toddler-sized toothbrush. This amount needs to be translated in Asian culturally appropriate language. Alternatively, markings on the toothbrush can be used to specify an equivalent amount.

• from 2 to 6 years: pea size or width of an age-appropriate toothbrush (0.25 g)

• 6 years of age and older: full thickness the length of the toothbrush (1 - 1.5 g)

The above recommendations are consistent with the WHO FDI IADR CSA 2007 Beijing Declaration: Call to Action to Promote Oral Health by Using Fluoride (FDI, IADR, and WHO, 2006). The fluoride dose is important with regard to enamel fluorosis in children under 6 yrs old, because very young children will ingest most of the toothpaste that is placed on the toothbrush and thus be exposed to fluoride systemically (Naccache *et al*., 1992). Wong *et al*. (2011) evaluated the risk for dental fluorosis when the use of fluoride toothpaste was begun in children younger than 12 months old; although fluorosis risk was indicated, the evidence was found to be weak and unreliable. From a risk/benefit perspective, preventing dental caries is likely to far outweigh the possibility of a minor cosmetic side-effect of mild fluorosis, and this is the basis for the recommendation above for fluoride concentrations in the range of 1000 to 1500 ppm F. Thus, reducing the amount of fluoride applied can be a better strategy than lowering the concentrations in toothpastes intended for use by children.

Brushing Time – Minimum of 2 minutes with a technique that encourages the dispersion of toothpaste around the teeth

The length of the brushing time (application phase) determines how long the relatively high fluoride concentration in the toothpaste slurry stays in contact with the teeth and plaque, allowing fluoride uptake to take place. A recent study has shown that increased brushing time increased fluoride concentrations in saliva for 2 hrs, as well as *in situ* enamel rehardening and fluoride uptake (Zero *et al*., 2010). Toothbrushing practices should promote optimal topical contact of the toothpaste slurry for the longest period of time. At the start of toothbrushing and before systematic plaque removal, the fluoride toothpaste should be rapidly spread around by the brushing of all occlusal tooth surfaces, and then swished between the teeth before the fluoride concentration has been diluted by saliva.

Assisted/Supervised Brushing up to Age 8 yrs – Parent/caregiver should control the amount of toothpaste placed on the toothbrush and the brushing time

The use of toothpaste should always be under adult supervision until the child is at least 8 yrs old, to achieve the desirable beneficial effects while minimizing possible adverse effects (fluorosis). Ideally, the parent/caretaker should apply the appropriate amount of toothpaste to the toothbrush and brush the child's teeth for an appropriate length of time (see above).

Post-brushing Behaviors – After brushing is completed, the toothpaste should be expectorated, and rinsing with water should be minimized

Rinsing behaviors after toothbrushing affect the amount of fluoride retained in the mouth (Zero *et al*., 1988, 1992b; Duckworth *et al*., 1991; Sjögren and Birkhed, 1993) and have been reported to affect caries experience (Chesters *et al*., 1992; Chestnutt *et al*., 1998; Sonbul and Birkhed, 2010).

Timing – Ideally, brushing should occur after meals, in the morning, and immediately before bed; other times of the day may also be appropriate in certain situations, i.e., *school-based brushing programs after lunch*

In general, the daily use of toothpaste should be performed at the time of the day that optimizes retention of fluoride in the oral cavity and minimizes clearance of fluoride. Behavioral factors such as eating and drinking after toothbrushing will accelerate the clearance of fluoride from the oral cavity, and thus toothbrushing should occur after eating and drinking and not before (Sjögren and Birkhed, 1994). Furthermore, bedtime use of fluoride toothpaste results in longer fluoride retention than daytime application, due to greatly decreased salivary flow during sleep (Zero *et al*., 1988, 1992b).

Affordability and Acceptance by the Public – Need for consideration as an essential public health measure; public health and community awareness programs; no or reduced tax rate

Results from the Cochrane topical fluoride review comparing one fluoride treatment with another (Marinho *et al*., 2004) indicated that children are more likely to persist with using toothpaste than with using any other topical fluoride treatment. Fluoride toothpaste should be considered as a dental health product, rather than a cosmetic, and therefore governments should be encouraged to reduce or remove taxation and tariffs for affordable fluoride toothpaste for their citizens (FDI, IADR, and WHO, 2006).

Encourage Oral Care Companies to Adopt These Guidelines in Their Advertising to the Public

To advocate the science-based effective use of fluoride toothpaste, oral care companies should be involved by adopting these guidelines in their advertising to the public. This will create a 'win-win' situation in that the public will repeatedly get the message on how to improve their oral health practices as companies make their products better known to the public. This could also be considered as a corporate social responsibility.

Aging Populations – Regular use of higher fluoride-concentration toothpastes (> 1500 ppm F) is recommended

High-fluoride toothpastes may be indicated for adults at higher risk for developing caries because of the insufficiency of caries control with conventional fluoride toothpaste and/or decreased salivary flow rate. There is some evidence that higher concentration-fluoride toothpaste (5000 ppm F) can help reverse root caries (Baysan *et al*., 2001).

Toothpaste Flavor – Should be acceptable to children but should not encourage swallowing

To encourage toothpaste use by children, the flavor should be mild, since children tend not to tolerate strong flavors. However, the taste should not be so good that it encourages children to swallow the toothpaste during brushing, or to lick or eat the toothpaste. Furthermore, strongly flavored toothpastes can stimulate salivary flow, leading to more rapid clearance of fluoride from the oral cavity (Bruun *et al*., 1987).

Use of Fluoride Toothpaste in Areas with High Fluoride – In agreement with the Beijing Declaration that "Fluoride toothpaste is safe to use irrespective of low, normal, or high fluoride exposure from other sources," if used as recommended

High fluoride levels in the environment (*i.e*., water, soil, coal, air) are the primary cause of endemic fluorosis. The contribution to total fluoride intake from fluoride toothpaste is extremely small in those areas with high fluoride levels from water, coal, and/or tea (FDI, IADR, and WHO, 2006).

Suggestions for Future Research in Asia

Several recommendations were made by the working group for future research on fluoride toothpaste:

• *Identification of appropriate fluoride concentrations for young children in a range of different environmental fluoride exposures*

• *Investigation of the best topical fluoride combinations*

• *Identification of fluoride methods that optimize the delivery of free (ionic) fluoride to plaque and actively demineralizing tooth surfaces*

• *Development of strategies that optimize the retention of fluoride in the oral cavity while minimizing fluoride ingestion*

• *Targeting fluoride treatment with the eruption patterns of teeth*

• *Investigation of fluoride use in combination with other remineralizing agents, such as calcium compounds and antimicrobial agents*

Fluoride Mouthrinses – Recommended for individuals at risk of developing caries

Concentration and Frequency – Both daily rinsing with 0.05% NaF (226 ppm F) and once-a-week/once-every-two-weeks rinsing programs with 0.2% NaF (909 ppm F) were found to be effective

Marinho *et al*. (2003b), in their systematic review, found that both daily rinsing with 0.05% NaF (226 ppm F) and once-a-week/once-every-two-weeks rinsing programs with 0.2% NaF (900 ppm F) were effective. However, although the effect of fluoride mouthrinse was not shown to be dependent on fluoride concentration and application frequency, a larger effect was indicated with increased intensity of application (frequency x F concentration); thus, considering the two most commonly used mouthrinse regimens, there might be limited choice, in terms of efficacy, when the weaker (230 ppm F) is used as a daily rinse and the stronger (900 ppm F) as a weekly rinse.

Rinsing Time – Ideally, 1 minute

The length of time for fluoride mouthrinsing is mainly based on *in vitro* fluoride update studies and is usually set at 60 sec, although 30-second rinsing times have been recommended for 4- to 6-year-old children (Ripa, 1991).

Formulation – Should be suitable for the age of the individual, i.e., taste should be age-appropriate (acceptable to children but not sufficient to encourage swallowing); alcohol may not be appropriate for some individuals, i.e., for children and patients with salivary dysfunction

Fluoride mouthrinse flavoring should be balanced between acceptability and not encouraging swallowing.

Age – Rinsing should start at age 4-6 yrs, depending on the level of supervision, to maximize the effect of fluoride on erupting permanent teeth

While the use of fluoride mouthrinse is generally recommended for children starting at age 6 yrs, there is evidence that, in Japanese children, fluoride mouthrinse can be safely used under supervision in 4- to 5-year-old children (Sakuma *et al*., 2004), and that this can lead to long-term benefits in caries prevention (Kobayashi *et al*., 1995). However, the importance of adult supervision cannot be overstressed.

Timing of Use – Rinsing should be used either following fluoride toothpaste use or independent of brushing

It is widely accepted that frequent applications of fluoride can be beneficial, and adding an additional fluoride exposure from a fluoride rinse may reduce caries in high-caries-risk individuals.

The use of a fluoride mouthrinse at concentrations of 0.05% NaF or above after brushing with fluoride toothpaste may also be advantageous for individuals who normally rinse with water after brushing, based on oral fluoride retention studies (Zero *et al*., 1988; Duckworth *et al*., 2009; Mystikos *et al*., 2011).

Assisted/Supervised Rinsing up to Age 8 yrs – Parent/caregiver should control the amount of mouthrinse dispensed and the length of the rinsing time

A Cochrane review (Marinho *et al*., 2003c) has shown that supervising a child's use of self-administered fluoride (toothpaste or mouthrinse) leads to greater benefits.

Suggestions for Future Research in Asia

Several recommendations were made by the working group for future research on fluoride mouthrinses.

- *Investigating the effect of fluoride mouthrinsing on primary dentition*
- *Timing of fluoride mouthrinse in relation to toothbrushing*
- *Combined effects of fluoride and anti-plaque agents*

FUTURE PROSPECTS FOR FLUORIDE USE

Fluoride will likely remain the cornerstone of caries control for the foreseeable future, because of its proven effectiveness and safety. However, there remains the need to determine the most effective method of fluoride utilization in children and adults who remain caries-active. Strategies that optimize the retention of fluoride in the oral cavity while minimizing fluoride ingestion will have obvious benefits. The use of fluoride in combination with anti-plaque and other remineralizing agents such as calcium as a pre-rinse or as a complex may have some potential; however, any agent that interferes with the ability of ionic fluoride to interact with a demineralizing tooth surface will likely be ineffective and possibly detrimental.

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