

# Systemic versus Topical Fluoride

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## Key Words

Caries prevention · Posteruptive fluoride · Pre-eruptive fluoride · Systemic fluoride · Topical fluoride

## Abstract

The actual mechanism of fluoride action is still a subject of debate. A dogma has existed for many decades, that fluoride has to be ingested and acts mainly pre-eruptively. However, recent studies concerning the systemic effect of fluoride supplementation concluded that the caries-preventive effect of fluoride is almost exclusively posteruptive. Moreover, epidemiologists have cast doubt on the validity of the 'old' studies dealing with fluoride use. The concept of the posteruptive fluoride effect is supported by in vitro and in situ investigations demonstrating that the mode of action of fluoride can be attributed mainly to its influence on de- and remineralization kinetics of dental hard tissues. Therefore, topical fluoride application (e.g. in the form of fluoridated dentifrices) should be encouraged. There are still important questions open that need to be answered despite existing knowledge about the caries-preventive effect of fluoride.

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## Existing Information

Fluoride is still the cornerstone of modern non-invasive dental caries management. However, the actual mechanism of fluoride action remains the subject of debate. The belief that fluoride has to be ingested and acts preventively by becoming incorporated into tooth mineral during its development originated from the early studies of Dean et al. [1942] and McKay [1952]. At this time many clinical trials were designed to prove the pre-eruptive (systemic) mode of action of fluoride. It could be demonstrated that the prevalence of overt carious lesions in the permanent as well as in the primary dentition was lower in residents from areas with fluoridated drinking water compared to those living in non-fluoridated areas [Backer Dirks et al., 1978; Thylstrup et al., 1982; Newbrun, 1989; Ripa, 1993]. Additionally, laboratory analyses revealed that fluoride concentration in surface enamel was higher in teeth that developed under the influence of water fluoridation [Chan et al., 1989; Takeuchi et al., 1996]. It was also found that the prenatal administration of fluoride supplements could reduce caries prevalence in deciduous teeth [Glenn et al., 1982]. As early as 1955, Bibby et al. compared the caries-preventive efficacy of fluoride lozenges with fluoride pills in a group of 5- to 14-year-old children. While the lozenges were sucked, the coated pills were swallowed before any of the contained fluoride could come into contact with the teeth. They

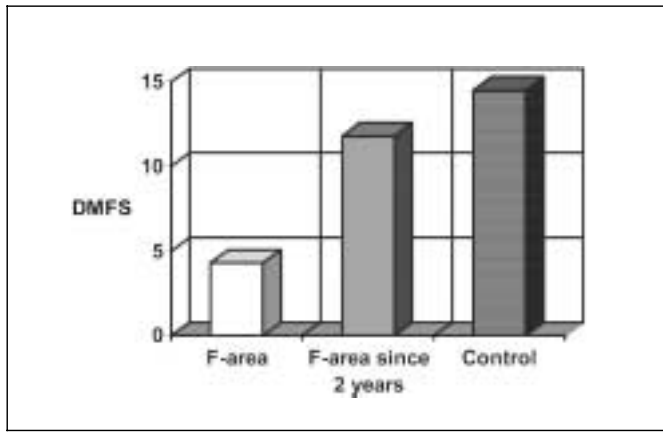
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**Fig. 1.** Mean DMFS scores of children (12.5–16.0 years) from three different areas: F area (naturally fluoridated drinking water since birth), F area since 2 years, and control (no fluoridated drinking water). Data from Hellwig and Klimek [1985].

were able to demonstrate that in the group using the lozenges fewer carious lesions developed compared to the group using the pills. They concluded that the caries reduction produced by such lozenges was the result of fluoride acting on the external surfaces of the teeth. Lemke et al. [1970] investigated the dental effects of discontinuation of controlled water fluoridation in Antigo (Wisconsin). They came to the conclusion that the (caries) inhibiting effect tends to persist as long as fluoride exposure is continued, but tends to be gradually lost after fluoride exposure is discontinued. They suggested that periodic or continuous renewal of the fluoride content of tooth enamel is required to maintain the maximum caries-inhibiting effect. However, these early indications of the posteruptive effect of fluoride were neglected and the dogma of the pre-eruptive mode of action of fluoride remained the basis for fluoride research. In this context, LeGeros et al. [1985] performed physicochemical investigations of enamel from deciduous teeth of a small number of children with and without prenatal fluoride supplementation. They found that enamel from children who were subjected to prenatal fluoridation exhibited more homogeneous and less extensive patterns of acid etching, denser crystal populations in intraprismatic regions, larger prism dimensions, greater total mineral density, a higher degree of crystallinity, smaller a-axis dimensions, more fluoride and less carbonate contents. These findings are always cited as evidence for the importance of systemic fluoridation, although they have not been verified since, particularly not for permanent teeth.

By the 1970s and 1980s, some doubts had emerged regarding the exclusively pre-eruptive effect of fluoride. Primary teeth were protected against caries even though prenatal incorporation of fluoride into unerupted teeth was insignificant. Additionally, a randomized, double-blind, longitudinal study testing the caries-preventing efficacy of prenatal fluoride supplementation in children followed until age 5 failed to support the hypothesis that prenatal fluoride has a strong caries-preventive effect [Leverett et al., 1997]. Hellwig and Klimek [1985] found that children 12.5–16 years old who had been exposed all their life to naturally fluoridated water exhibited significantly fewer carious lesions compared to a control group. However, they also found that even children who consumed fluoridated water for only for 2 years showed a distinctly decreased DMFT score compared to the control children (fig. 1). Künzel and Fischer [1997] analyzed the rise and fall of caries prevalence in two German towns and its relationship to changing drinking water F concentrations. During the first three decades of the study the caries prevalence correlated strictly with the F concentration in the drinking water. Water fluoridation was followed by a caries decline, while interruptions in fluoridation were followed by increasing caries levels. However, since 1987 a significant caries decline occurred despite the fact that only poor water fluoridation was available. They concluded that one of the reasons might be the broader availability of other fluoride-containing products compensating for water fluoridation, e.g. F dentifrices. A similar result was reported by König [2001] for the Netherlands. From 1953 to 1973, drinking water in Tiel was fluoridated and consequently children aged 12 years had significantly lower caries prevalence if compared to children from a control town, namely Culemborg. However, caries prevalence decreased gradually in both towns during the subsequent years and by 1980 was in quite the same order for both towns. He concluded that there is no need for ‘systemic fluoridation’ when topical fluoride application is available, e.g. as fluoridated dentifrices. About 10 years later, Groeneveld et al. [1990] recalculated the Tiel-Culemborg data and came to the conclusion that there was some pre-eruptive fluoride effect especially in pits and fissures. However, Limeback [1999] questioned their estimates since they did not offer any error analyses. Reich et al. [1992] investigated the caries prevalence of 5-year-old children, who had been subjected to different regimens of fluoride supplementation. One group received fluoride supplements from birth, the other group starting from 7 months. There was no statistically significant difference in dmfs scores in the primary teeth

at age 5, indicating that fluoride exerts a posteruptive effect and that fluoride 'supplementation' starting from birth is unnecessary. Stephen and Campbell [1978] were able to demonstrate a considerable caries-reducing effect for fluoride tablets when they are sucked and fluoride is allowed to act topically. All the above-mentioned clinical studies suggest that fluoride action is predominantly posteruptive. When reviewing the pre- and posteruptive effects of fluoride, Burt [1999] came to the conclusion that the cariostatic benefit of continuous fluoride exposure in a community is cumulative, i.e. fluoride has its effect by other means than pre-eruptive incorporation into the hydroxyapatite crystal. Otherwise caries-preventive benefits should be maximized in a group of children born when water fluoridation began and caries prevalence would not drop further as a result of water fluoridation. But epidemiological studies demonstrated a further decline in caries prevalence in subsequent cohorts, although no additional fluoridation measure was available [Arnold, 1957; Johnston et al., 1986].

At the same time laboratory studies came to conflicting results. While some could demonstrate that the solubility of enamel originating from residents of a fluoridated region was low, the others could not confirm these results and no direct correlation between fluorapatite in enamel and caries levels in populations could be demonstrated [Armstrong and Brekhus, 1938; Mellberg and Ripa, 1983]. Moreover, it was reported that even shortly after eruption the surface enamel is partly abraded physiologically and fluoride-rich enamel is lost [Aasenden, 1975]. Consequently, it seemed inconceivable that a rather low increase in surface enamel fluoride content due to fluoride ingestion could explain the caries-preventing efficacy of fluoride supplementation. In this context, Ögaard [1990] demonstrated that even shark enamel consisting mainly of fluorapatite demineralizes in an intra-oral caries model. He could also show that topical application of fluoride inhibits the development of caries lesions in human enamel, while it did not interfere with demineralization of shark enamel. The results of more recent epidemiological and laboratory studies can be summarized by stating that posteruptive (topical) application of fluoride plays the dominant role in caries prevention. It may be argued that fluoride might be recycled via the salivary glands after systemic administration, thereby affecting the rate of progression of caries lesions. Oliveby et al. [1989] investigated fluoride excretion in human saliva and its relationship to plasma fluoride levels after ingestion of 1 mg fluoride as NaF. The fluoride concentration in saliva is 2/3 that in simultaneously collected plasma

and this relationship is maintained when fluoride is ingested [Ekstrand and Oliveby, 1999]. About 40 min after fluoride intake, the peak fluoride concentration in saliva is reached. After 120 min, salivary fluoride concentration decreases distinctly and it is unlikely that the small amount of fluoride recycled into the oral cavity per se can exert a significant caries-preventive effect. However, since plaque can accumulate fluoride [Dawes et al., 1965; Grobler et al., 1982; Ekstrand and Oliveby, 1999], it is conceivable that increasing the salivary fluoride concentration might be of some importance. But even if this is the case, it would be more advisable to increase plaque fluoride concentration directly by topical application.

More recently, epidemiologists have questioned the validity of the 'old' studies dealing with systemic fluoride use. Since epidemiology was less advanced as a science, many cross-sectional studies were biased. Different grades of oral cleanliness, use of additional fluorides, selected or self-selecting groups, lack of examiner blindness, no concurrent controls, high dropout rates, retrospective analysis, differences in caries activity, no randomization, and different levels of dental awareness were some of the inherent interfering factors [Burt, 1999; Riordan, 1999]. Today it is well accepted that long-term exposure to topical fluorides mediates a reduction in caries prevalence similar to that obtained through 'fluoride supplementation'. Clinical findings are supported by *in vitro* and *in vivo* studies demonstrating that the mode of action of fluoride can be mainly attributed to its influence on the de- and remineralization kinetics of dental hard tissues [Fejerskov et al., 1981; ten Cate and Featherstone, 1991; ten Cate, 1999]. Thus, fluoride should be present in the oral cavity throughout life, particularly during the period when the teeth are erupting [Thylstrup, 1990]. However, in the clinical situation the optimum fluoride level to prevent caries development is not known.

In conclusion, one must state that to date there is no placebo-controlled, randomized, prospective study available determining how much of the anticaries effect can be attributed to pre-eruptive or posteruptive fluoride. However, carefully considering the present evidence from clinical and laboratory studies, it can be concluded that the caries-preventive mode of action of fluoride is mainly posteruptive. An entirely different problem with fluoride supplementation has been pointed out by Clark [1993]. He came to the conclusion that fluoride supplements are not particularly effective because of compliance problems. It should also be taken into account that fluoride supplementation increases the risk of fluorosis [Thylstrup et al., 1979; Riordan, 1993, 1999].

## State of the Art

The daily use of an optimally formulated fluoride-containing dentifrice offers the chance for optimum caries prevention on a community and individual level, since it combines oral hygiene with fluoride supplementation. Moreover, this advice follows the idea that small amounts of fluoride should be present during a caries attack. Fluoride-containing mouthrinses, varnishes and gels offer an additional opportunity for caries prevention among people with moderate and high caries activity. Fluoride tablets or lozenges can be used as an aid for topical fluoride application, when children or adults are not able or willing to brush their teeth with a fluoridated dentifrice. People using them should be advised to suck them slowly and not to swallow them immediately after application. In areas with fluoridated drinking water the application of fluoride tablets is not advisable for toxicological reasons. The use of fluoride dentifrices by children living in these areas should be limited to those who are able to spit out adequately after toothbrushing.

## Future Perspectives for Research

In 1999 an international panel of scientists considered 10 priorities concerning fluoride research at large [Clarkson, 2000]. Focusing on the topic of the present paper the following, additional questions are still unanswered: Is there a difference with respect to caries development and caries progression between a group of children who used fluoridated dentifrice since the eruption of the first deciduous tooth and a group of children who used coated tablets since birth and brushed their teeth with an non-fluoridated dentifrice? Is there a measurable effect of fluoride 'supplementation' on tooth morphology resulting in a measurable caries-preventive effect? Does fluoride supplementation really promote body growth and/or formation of more stable bone architecture? Is caries development or lesion progression influenced by topical application of fluoride? What is the optimum fluoride concentration for topical treatment under clinical conditions?

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