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# The Pre- and Posteruptive Effects of Fluoride in the Caries Decline

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## Abstract

*The widespread availability of fluoride from many sources is accepted as a major reason for the caries decline among children in developed countries. There is still controversy, however, about its principal mode of action. This article reviews the evidence on fluoride's preeruptive and posteruptive effects, and suggests reasons for its continuing role in the caries decline. Early fluoridation studies accepted that fluoride acted preeruptively through incorporation into developing enamel; but further research could not explain why fluoride levels were not clearly higher in enamel exposed to fluoride, nor why there were no clear correlations between caries experience and enamel fluoride concentration. Instead, considerable evidence suggests that fluoride acts mainly, though not entirely, through posteruptive remineralization of demineralized enamel. Caries experience has declined in non-fluoridated as well as in fluoridated areas, though DMF scores are still consistently lower in fluoridated areas. Posteruptive remineralization effects are seen from fluoridated drinking water as well as with fluoride from other sources. The continuing caries decline, beyond the level suggested by early fluoridation field trials, can be attributed either to more efficient remineralization or to long-term, intraoral ecological change, or to both.*

**Key Words:** fluoride, fluoridation, caries, enamel, epidemiology

## Introduction

After some hint of the caries decline among children during the mid-1970s (1,2), a series of reports confirmed it in a number of economically developed countries soon after (3-12). The global nature of the decline was documented at the First International Conference on the Declining Prevalence of Dental Caries at the Forsyth Dental Center, Boston, the proceedings of which were published as a special issue of the *Journal of Dental Research* in November 1982. The reports listed in

Table 1 constitute the bulk of the evidence for the caries decline in economically developed countries.

The beginning of the caries decline cannot be specified precisely, though it may have been before the 1970s (13,14). Nor can the reasons for the decline be stated with certainty; many diseases have surged and declined throughout history for unknown reasons (15). Some specific causes that have been suggested, though with supporting evidence that is not always compelling, include decline in consumption of sugars, widespread use of antibiotics, improved vitamin and mineral consumption, and improved dental care. Other potential causative factors, though they cannot be documented, include bacterial and immunological changes. The reason most often suggested for the caries decline is the widespread use of fluoride. Water fluoridation reportedly is practiced to some extent in over 30 countries since it began in 1945 (16), fluoride toothpastes became a major component of the toothpaste market during the 1970s (17), and dentists around the world have been dispensing fluoride supplements and mouthrinses for years.

Water fluoridation was the original public health application of fluoride, and it remains the most contentious. There have long been divergent views on whether water fluoridation prevents caries primarily through preeruptive systemic uptake by developing enamel, or by posteruptive remineralization and various antibacterial effects (18,19). The issue is worth exploring further, since better understanding of its mode of action will influence public policy and recommended use of all forms of fluoride. This article reviews the evidence relating to fluoride's preeruptive and posteruptive effects on dental enamel, and suggests hypotheses to explain why frequent fluoride exposure is a primary cause of the continuing decline in caries among children in countries where it is in common use.

## Early Studies

Reports of the initial fluoridation field trials included little discussion about the mechanism by which fluoride acted, but it was implied that fluoridation was effective principally because fluoride was incorporated into developing enamel to form a "stronger" or "more acid-resistant" fluorapatite crystal (20,21). In 1952, re-

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Send correspondence and reprint requests to Dr. Beltran. This study was supported by a contract from the Dental Disease Prevention Activity, Centers for Disease Control, Atlanta, Georgia. Manuscript received: 12/29/87; returned to author for revision: 2/26/88; accepted for publication: 4/20/88.

**TABLE 1**  
**Selection of Reports Since 1979 Describing Reductions in Caries Among Children in Different Countries (Field Trials of Water Fluoridation Not Included)**

| Authors                    | Year | Location      | Reduction                                      |
|----------------------------|------|---------------|------------------------------------------------|
| Peterson (121)             | 1979 | North Dakota  | 38% over 5 years, 8-12-year-olds               |
| Zacherl and Long (122)     | 1979 | Ohio          | 22% over 6 years, 12-year-olds                 |
| Mansson et al. (3)         | 1979 | Sweden        | 53% over 10 years                              |
| McEniery and Davies (4)    | 1979 | Australia     | 50% over 20 years, 10-14-year-olds             |
| Hugoson et al. (5)         | 1980 | Sweden        | approximately 50% over 5 years, 3-20-year-olds |
| Anderson (6)               | 1981 | England       | 36% over 15 years                              |
| Anderson (7)               | 1981 | England       | 32% over 10 years                              |
| Anderson et al. (8)        | 1981 | England       | 51% over 15 years                              |
| Milen et al. (10)          | 1981 | Finland       | 54% over 5 years                               |
| USPHS (12)                 | 1981 | USA           | 36% over 6-8 years, 5-17-year-olds             |
| Backman et al. (123)       | 1982 | Sweden        | 33% over 12 years                              |
| Bristow et al. (124)       | 1982 | England       | approximately 35% over 6 years, 12-year-olds   |
| Bryan et al. (125)         | 1982 | Tennessee     | 54% over 25 years, 6-14-year-olds              |
| Carr (126)                 | 1982 | Australia     | 26% over 3 years                               |
| Latcham et al. (127)       | 1982 | Australia     | 50% proximal 4-5 years                         |
| Silver (128)               | 1982 | England       | 62% primary 8 years                            |
| Fejerskov et al. (129)     | 1982 | Denmark       | 27% over 7 years, grade 1                      |
| O'Mullane (130)            | 1982 | Ireland       | 54% over 19 years                              |
| Kalsbeek (131)             | 1982 | Netherlands   | 50% over 10 years                              |
| Brown (132)                | 1982 | New Zealand   | 39% over 5 years                               |
| von der Fehr (133)         | 1982 | Norway        | 50-70% over 10 years                           |
| Glass (134)                | 1982 | Massachusetts | 55-70% over 20 years                           |
| DePaola et al. (135)       | 1982 | Massachusetts | 50% over 28 years, grades K-11                 |
| Allen et al. (136)         | 1983 | England       | 49% over 19 years, from x-rays                 |
| Clerehugh et al. (137)     | 1983 | England       | 25% over 8 years, 11-12-year-olds              |
| Hargreaves et al. (138)    | 1983 | Scotland      | 32-60% over 10 years, 8-14-year-olds           |
| Hausen et al. (139)        | 1983 | Finland       | 6% over 4 years, 12-year-olds                  |
| Sposato et al. (140)       | 1983 | New York      | 47% over 5 years, fluoride rinse               |
| Hanzely et al. (141)       | 1985 | Hungary       | 8% over 7 years, preschool                     |
| Møller (142)               | 1985 | Iceland       | no change in DMF over 13 years                 |
| Stookey et al. (143)       | 1985 | Indiana       | 70% over 23 years, grades 1-12                 |
| Truin et al. (144)         | 1985 | Netherlands   | 57-76% over 12 years, 7-year-olds              |
| Mansbridge and Brown (145) | 1986 | Scotland      | 26% over 16 years                              |

duction of enamel solubility was listed as the first of four theories on how fluoridation prevented caries, and a nonspecified topical action was the fourth (22). This view probably reflected the extensive research into hydroxyapatite chemistry and crystallography that began during the 1940s. (The other two theories listed were salivary action and inhibition of bacterial and enzymatic processes.) Even with applications of high-concentration topical solutions, early studies were interpreted as showing that the fluoride was incorporated into enamel as fluorapatite with only a small amount forming calcium fluoride on the enamel surface (23).

A natural corollary of the "stronger enamel" view was that full benefit from fluoridation came only when children were drinking fluoridated water from birth, thus receiving maximum preeruptive uptake during the period of tooth development (24). Even though a number of early reports showed that teeth already erupted benefited when fluoridation began (25-28), all concluded that the earlier that fluoridation began for

each cohort, the greater the anticariogenic effect. In the dental literature from the 1940s and early 1950s, the only questioning of whether action of fluoride resulted from preeruptive uptake was reported to have come from Volker in 1940 (22).

#### Preeruptive Enamel Effects

It was long assumed that maximum benefits from fluoridation were seen in the first cohort to consume fluoridated water from birth: "Children aged 5-8 years, with the use of fluoridated water from birth, apparently exhibit the ultimate degree of inhibition" (29). When evidence showed that fluoridated water benefited adults (30-32), the conclusion was that "fluoridation's benefits extend into adulthood." The dominance of the preeruptive view at the time is demonstrated by the design of these last three adult studies: all were restricted to permanent residents of the fluoridated areas, suggesting that the question of posteruptive benefits did not arise.

Fluoride ingested prior to tooth eruption is partly incorporated into tooth enamel, mostly during the preeruptive maturation period (33). The amount of fluoride deposited preeruptively depends on its concentration in food, water, or supplements ingested (34), the duration of the ingestion period (35), and the length of the preeruptive maturation stage (36,37). The principal benefits of preeruptive ingestion are considered to be improved crystallinity and reduced enamel solubility (38).

Apatite is typically a small, impure crystal, though fluoride effectively increases its crystallinity in bones and teeth (39). Improvement in crystallinity produces a thermodynamically more stable crystal that is more resistant to acid-dissolution, less impure, and possibly dimensionally bigger. In this regard, there is evidence that fluoride acts as a catalyst during mineralization, causing transformation of the more soluble precursors (octocalcium-, tricalcium-, and dicalcium phosphates) into a thermodynamically more stable apatite (40). It has also been suggested that fluoride might stabilize the apatite crystal through stronger hydrogen bonds (41,42); an inverse carbonate-fluoride relationship in enamel has also been suggested (43-45).

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The presumed benefit from fluoride's reduction of enamel solubility is based on studies that reported higher concentrations in teeth from fluoridated as against nonfluoridated areas (46-50), and the in vitro observation that fluorapatite is less soluble than hydroxyapatite when exposed to acids (51-53). Several recent studies, however, have detected only slight differences in enamel fluoride concentration between fluoridated and nonfluoridated areas (54-56), and no differences could be detected between groups of Danish children who did or did not take fluoride supplements prior to tooth eruption (57). Earlier, it had been suggested that incorporation of fluoride only into the outermost layers of enamel was sufficient to permit all the enamel to behave as fluorapatite (58).

But even before these recent studies, it became apparent to some observers that a higher fluoride content of enamel could not by itself explain the considerable reductions in caries that fluoride brought about (59); the difference in enamel fluoride concentrations between fluoridated and nonfluoridated areas was simply insufficient. The theoretical concentration of fluoride in pure

fluorapatite, which would produce a substantial reduction in acid solubility, is around 38,000 ppm (38,59); but recorded values from an enamel depth of two microns are only in the order of 1,700 ppm in nonfluoridated areas, 2,200-3,200 in 1 ppm fluoridated areas, and 4,800 ppm in an area with a water fluoride concentration of 5-7 ppm (60). These latter concentrations have also been found in the outermost enamel layers of people from low-fluoride areas (39).

If the elevated fluoride concentration in enamel from fluoridated areas is an important factor in caries prevention, then there should be a relation between enamel fluoride levels and caries experience. But results from a number of studies on this issue are contradictory. Significant but weak inverse relationships between surface enamel fluoride and DMF scores have been found among groups (37,56,61-64), but not at the individual level (63,65,66). A number of other studies, both in vivo and in vitro, have failed to demonstrate any relationship between enamel fluoride levels and caries experience in primary and permanent dentitions (67-73). Comparability of results from these studies is hampered by the different techniques employed for enamel biopsy, the variability in sample depths, and the different assumptions on calcium concentration in enamel and enamel density among the studies. Moreover, the fluoride concentration in the buccal surfaces of the incisors and premolars sampled for these studies may not represent fluoride concentration in the enamel of pits and fissures where caries usually begins.

Despite this equivocal relationship between enamel fluoride and DMF scores, some recent epidemiologic evidence joins the earlier studies to suggest that preeruptive fluoride effects are observable. Driscoll et al. (74), in their study of long-term benefits from supervised ingestion of fluoride supplements, found greater benefits to teeth that were unerupted at the time of the supplement program. In their study of children residing in a nonfluoridated area, Burt et al. (75) found slightly less caries in permanent teeth among children who had previously lived for varying periods in fluoridated areas prior to eruption of the first molars.

#### **Posteruptive Enamel Effects**

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As mentioned before, early fluoridation studies reported dental benefits to teeth that had already erupted at the time fluoridation began (25-28). Another study from this period found that children who moved to a fluoridated area prior to eruption of the first molars received the same benefits to the permanent teeth as did the original residents, regardless of the age at which the newcomers moved (76). Data from other studies indicated that continuing topical exposure to fluoride from drinking water was necessary to maintain anticaries effects (77,78). While the results of Burt et al. (75) suggested a contrary effect, this latter study was in an age when toothpaste was a common source of continuing exposure to topical fluoride, whereas Russell's and the Antigo study were not. A British report from 1982 specifies clear benefits to teeth already erupted when fluoridation began (79), and recent Danish stud-

ies also support posteruptive fluoride effects (80-83).

Although crystallinity improvement and decreased solubility are phenomena that occur both pre- and post-eruptively (45), the major posteruptive effect of fluoride on dental enamel is remineralization of previously demineralized enamel (38,59).

Remineralization has been defined by Arends and Gelhard (84) as "the deposition of mineral in enamel defects." Remineralization is a natural defense mechanism, as evidenced by human saliva's ability to promote remineralization by itself (85-87). Remineralization was concluded to be the cause of the arrest, or even the reversal, of early carious lesions in early fluoridation clinical trials (88,89), as well as in lesions produced experimentally in vivo (90). Fluoride content of highly porous or previously "primed" enamel, such as that found in recently erupted enamel or white spot lesions, is much higher than that in adjacent sound enamel (91-94). When teeth with such lesions are subjected to a slightly acidic environment, mineral dissolves from subsurface regions of the sound enamel, but not from the remineralized areas (95).

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Enhancement of this process, using both natural and artificial carious lesions, has been reported by several workers in vitro (96-103) and in vivo (84,104-108). The presence of fluoride in trace quantities is critical to the remineralization process (49,97,101). If fluoride is present at the time of acid challenge, it will diffuse with the acid and inhibit dissolution at the crystal surface; if it is present during remineralization it enhances crystal growth and hence makes the overall remineralization process more rapid and effective (109). The source of the fluoride can be plaque fluid (110) or surface enamel.

Because remineralization is promoted by the frequent introduction of low-concentration fluoride into the oral environment (103), the small amount of fluoride in fluoridated drinking water is sufficient to promote remineralization. The requisite fluoride level can be obtained from fluoridated water at least as well as from other commonly used agents like toothpaste (38), though fluoride toothpaste is probably the main source of fluoride for remineralization in nonfluoridated areas (103). In fluoridated areas, fluoride from water supplies and from dentifrice may exert an additive effect, though this issue has received little epidemiologic study.

Where there is constant intake of low-concentration fluoride, from whatever source, the evidence suggests that a fluoride "reservoir" develops in plaque and remineralized subclinical lesions, from which fluoride is constantly being released in response to demineralization. The result is a continuing cycle of demineralization and subsequent remineralization to maintain enamel integrity. Only when demineralization overwhelms the defense mechanisms does clinical caries develop.

### **Epidemiologic Studies**

If the principal (though not the sole) action of fluoride is posteruptive, then caries experience in communities with long-standing and comprehensive topical fluoride programs should, in time, approach that of communities where the drinking water is fluoridated. Data to suggest such a trend have been reported from Denmark (111) and from Canada (112). On the other hand, data from the 1979-80 National Dental Caries Prevalence Survey in the United States have been used to show that a considerable gap in caries experience still remains between fluoridated and nonfluoridated communities (113). These arguments are worth closer examination.

Thylstrup et al. (111) analyzed cross-sectional DMF data for the period 1972-80 from four areas of Denmark with differing concentrations of naturally occurring fluoride in the drinking water. Vordingborg (1.2 ppm) is a stable rural community, while Ballerup (0.4 ppm) and Hvidovre (0.4 ppm) are rapidly growing suburbs of Copenhagen. Skibby (0.5 ppm) is a small stable rural community in which the school dental service was established more recently than in the other communities. Thylstrup et al. found that DMF scores in fluoridated Vordingborg had declined only slightly over the 1972-80 period, while those from Ballerup and Hvidovre had declined sharply. DMF scores in Skibby declined moderately. The end result was that the initial 1972 gap in DMF scores between the fluoridated and nonfluoridated communities had been considerably narrowed, though DMF values were still a little lower in fluoridated Vordingborg. The authors concluded that the convergence of DMF scores was due to the generalized use of topical fluoride (toothpastes, rinses), both at home and through the school dental service.

Although this conclusion is plausible, the direct comparison between Vordingborg and the two suburban areas is hardly valid. The authors state that the population of each of the Copenhagen suburbs increased from around 20,000 in 1960 to about 50,000 at the time of writing. Assuming linear growth rates, this would mean about 50 percent growth in the period under study, 1972-80. In this sequential cross-sectional study, such rapid growth means that each suburb's apparent reduction in dental caries between 1972 and 1980 could have resulted as much from the influx of persons with excellent oral health as it did from improvements in the original residents. Thylstrup et al. (111) further argued that the posteruptive action of fluoride from toothpaste and from organized mouthrinsing programs makes wa-

ter fluoridation unnecessary. That essentially political viewpoint invokes issues beyond the scope of this article, but the investigations presented no evidence to negate posteruptive effects from fluoride in drinking water.

In Canada, Johnston, Grainger, and Ryan (112) demonstrated that there was a marked caries decline in Ontario children in the 1972-84 period, and even suggested that it may have begun as early as the 1950s. They proposed that the widespread use of topical fluoride and water fluoridation, which reaches 72 percent of Ontario's population, as the most likely reasons for the decline. In Perth County, where 98 percent of the population drink water naturally fluoridated at optimum or above-optimum levels, the DMF for 13-year-olds fell from about 5.5 in 1972 to about 2.8 in 1984 (estimated from graph), this latter figure being still below the average for the province. The authors noted that caries declined by the same relative amount over time in fluoridated and in nonfluoridated areas. Like the report from Thylstrup et al. (111), this paper suggested nothing to oppose a posteruptive effect of fluoride from drinking water. Also as seen in the Danish report, caries experience was lower and continuing to decline in the fluoridated areas.

Brunelle et al. (113) used residential histories for children in the 1979-80 national survey in the United States to compare those with lifelong fluoridation ingestion against those with none. Children aged 5-17 who had received fluoridated water for their whole lives recorded 33 percent fewer DMFS lesions than those without fluoridated water. The magnitude of this difference is greater than that found in the Danish and Canadian studies; but since the potentially confounding effects of age-distribution and socioeconomic differences were not detailed (113), it cannot be taken too literally.

Regardless of the political point of view implied, these epidemiologic studies all indicate that the anticariogenic effects of fluoride continue over long periods of time. Some reasons for this phenomenon can now be hypothesized.

#### **Reasons for Continuing Anticaries Fluoride Action**

There is no evidence that the caries decline has yet "bottomed out." If fluoride is largely responsible for the decline, this observation supports the view that its action continues beyond that to be expected solely from the results of short-term clinical trials, or even from the fluoridation field trials. Other reviewers have reached the same conclusion (18,38,59).

One possible explanation is that fluoride is increasingly available from more sources, so that low-concentration fluoride is being introduced into the mouth more and more frequently from drinking water, toothpaste, mouthwashes, foods, and professional dental applications. Fluoride stored in surface enamel, plaque, and to some extent in saliva and on mucous membranes, is therefore always available when needed, meaning that remineralization is continually becoming more efficient.

In addition, more subtle changes in the ecology of the oral cavity may promote the continuing decline. Caries is a transmissible disease, with *Streptococcus mutans* being transmitted to the mouths of infants soon after tooth eruption (114). Fluoride can interfere with this transmission by reducing *S. mutans* levels in mothers of infants, so that there are fewer bacteria to transmit (115,116). In addition, low-concentration fluoride has been shown in vitro to induce *S. mutans* to become less cariogenic through adaptation (117,118). Some years of widespread fluoride use in the economically developed world could have induced oral ecological change at a population level, and may be continuing to do so. The "hostile environment" for cariogenic bacteria created by widespread and long-term use of fluoride (119) may now be the norm in many communities.

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These hypothesized bacterial effects from low-concentration fluoride are more subtle and long-term than the direct bactericidal effects of high-concentration fluoride (120), and they could set up a compounding effect as time goes by; existing cariogenic bacteria diminish in cariogenicity, so less cariogenic bacteria are transmitted, then continuing use of fluoride reduces cariogenicity even further, and so on.

Either or both of the mechanisms described—i.e., more efficient remineralization or ecological change—are plausible explanations for why caries reductions have exceeded the levels to be expected from clinical trials, and why the anticaries effects of sustained fluoride use in a community are not maximized in the first cohort of children born after fluoridation begins.

#### **Conclusion**

The widespread availability of fluoride from various sources in developed countries has contributed to the reduction of dental caries in children. Water fluoridation and fluoride dentifrices are the major sources of continuous fluoride action within the oral cavity. While evidence supports both preeruptive and posteruptive fluoride effects, current research favors a greater role for posteruptive fluoride. More efficient remineralization and ecological changes are both good reasons why fluoride induces continuing reductions in caries in countries where fluoride is widely used.

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