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The Case for Eliminating the Use of Dietary Fluoride Supplements for Young Children

Brian A. Burt BDS, MPH, PhD

Abstract

Fluoride supplements have been used for years to prevent dental caries; nevertheless, there are three reasons why their use is inappropriate today among infants and young children in the United States. Evidence for the efficacy of fluoride supplements when used from birth or soon after is weak, supplements are a risk factor for dental fluorosis, and fluoride has little preeruptive effect in caries prevention. While there are many reports on the caries-preventive efficacy of supplements, few meet standards for acceptability as clinical trials, and those that do have tested chewable tablets or lozenges under supervision in school-aged children. North American children today are exposed to fluoride from many sources—drinking water, toothpaste, gels, rinses, and in processed foods and beverages. The additional cariostatic benefits that accrue from using supplements are marginal at best, while there is strong risk of fluorosis when young children use supplements. Available evidence suggests that the public is more aware of the milder forms of fluorosis than was previously thought; thus, it is prudent for caries-preventive policies to aim at maximizing caries reductions while minimizing the risk of fluorosis. It is therefore concluded that the risks of using supplements in infants and young children outweigh the benefits. Because alternative forms of fluoride for high-risk individuals exist, fluoride supplements should no longer be used for young children in North America. [J Public Health Dent 1999;59(4):269-74]

Key Words: fluoride, dietary fluoride supplements, infants, children, caries, fluorosis, prevention.

Fluoride supplements come in the form of tablets or drops intended to be swallowed, tablets for chewing, or lozenges for sucking and slow intraoral dissolution. They contain a measured amount of fluoride, typically 0.25 mg, 0.5 mg, or 1.0 mg. These products have been used to prevent dental caries among children in many countries since around 1950. Fluoride supplements were introduced as a substitute for fluoridated water among children in nonfluoridated areas, and are intended for use only in areas where there is little or no fluoride in the drinking water.

The Council on Dental Therapeutics of the American Dental Association (ADA) stated in 1978 that maximum caries protection is afforded, with virtually no risk of fluorosis, when supplements are taken from birth according to the recommended schedule (1).

Another review, a few years later, concluded that dietary fluoride supplementation, when used in accordance with recommendations, is a "patently safe and highly effective measure for the prevention of dental caries" (2). The sense of this statement has formed the basis for policies on supplement use in the United States up to the present time.

When supplements were first introduced, it was assumed that fluoride's cariostatic effects were largely preeruptive. This belief was summarized in a 1958 ADA report, which stated: "Since it appears that dietary fluoride provides its greatest benefit during the period of tooth development, one may assume that the child should receive adequate fluoride until at least 8 to 10 years of age" (3).

The same report went on to state that prescription fluorides were not

beneficial to adults. The directions for use of the supplements, in low water-fluoride areas, were that the 1.0 mg fluoride tablet should be dissolved in a quart of water for drinking purposes and food preparation for children up to 2 years old. For children between 2 and 3 years of age, a tablet (1.0 mg fluoride) was to be administered every other day in fruit juice or water to be consumed at one time. After 3 years of age, the recommendation was that the tablet be administered daily in fruit juice or water to be drunk at one time (3).

These recommendations use virtually the same amounts and timing as current recommendations. However, much has changed since 1958. The extent and severity of caries has declined, fluoride uses have multiplied, our knowledge of how fluoride works to inhibit caries has advanced, we know more about tooth development, and we are more concerned about fluorosis. In fact, things have changed so much that the use of fluoride dietary supplements for young children now presents more problems than benefits. In saying that, I accept that a fluoride supplement, made to be dissolved in the mouth slowly over a long period, could be a valuable fluoride therapy for older children with a caries problem, or even for adults of any age. These latter issues wait to be investigated further. For now, this paper will discuss three reasons why fluoride supplements have become inappropriate for use among infants and young children in the United States. Those reasons are: (1) Little firm evidence exists for the efficacy of dietary fluoride supplements when taken from birth or soon after. (2) Fluoride supplements are a risk factor for fluorosis. (3) The preeruptive cariostatic benefits of fluoride are minor.

Efficacy of Fluoride Supplements in Young Children

As a general statement, the literature shows that children who use fluoride supplements from birth or soon after have less dental caries than children who do not. However, the cause-and-effect relationship is much less clear. With few exceptions, the literature to support the benefits of supplements demonstrates only associations, and design flaws in these reports are common. Some of these problems can be found in a 1978 review (4) in which a number of the studies reviewed used selected groups of participants, employed no concurrent controls, and suffered from severe attrition of subjects. This review concluded that caries reductions of 50 percent to 80 percent were attainable in the primary dentition and 20 percent to 40 percent in the permanent dentition through the use of fluoride supplements. This conclusion could be questioned because a number of the studies reviewed found either marginal or no reductions in caries. These concerns have been described previously in greater detail (5).

There are, however, other frequently quoted reports in which design problems are severe enough to cast doubt on the validity of the results. In a retrospective study, Aasenden and Peebles (6) reported an 80 percent reduction in caries in the permanent dentition among children who used fluoride supplements from birth, compared to children who did not use supplements at all. The children who used the supplements from birth also exhibited 50 percent less caries than did children who were lifelong residents of a fluoridated community. Not only was there no random allocation of subjects (all of whom were pediatricians' patients), but also a serious bias was introduced by self-selection of members of the fluoride supplement group. The likelihood that group allocation was biased was strengthened by the finding that oral cleanliness was significantly better among those children taking the supplements, and by the fact that this group included significantly more girls than the other two. Lesser issues included the non-mention of examiner blindness and evidence that the water supply for the second control group was not optimally fluoridated. The bias in subject allocation is serious enough to cast

doubt on the validity of the results. Similar problems were evident in another study from the mid-1970s, this one a 10-year prospective study of children living in two communities in different states (7).

An early study carried out by the US Public Health Service (USPHS) concluded that the results from use of fluoride supplements were similar to those achieved with water fluoridation (8). But this study was not a clinical trial—the participants were selected children of USPHS professionals, it had no concurrent controls, compliance with an awkward dosage schedule was not assured, and fewer than half of the original participants completed the project. Despite these weaknesses, the results of this study formed the basis for subsequent USPHS policy on the use of fluoride supplements.

Well-conducted clinical trials for supplement efficacy have been confined to school-based studies. Driscoll and colleagues (9) in Wayne County, NC, found a 28 percent reduction in caries of the permanent dentition over six years when supplements were chewed, swished, and swallowed by schoolchildren under supervision. Concurrent controls, placebos, and double-blind conditions were part of the design. Caries reductions were higher for those teeth erupting during the study, and beneficial effects were still discernible four years later (10). Results similar to those from Wayne County had earlier been reported from a well-conducted, school-based, clinical trial over three years in the Boston area (11). More spectacular results—an 81.3 percent reduction in caries incidence—were reported from a Glasgow study in which children initially aged 5.5 years from lower socioeconomic groups sucked a 1.0 mg fluoride tablet, or a placebo, under supervision in schools every school day for three years (12). The benefits were almost all seen in the erupting first permanent molars.

Retrospective analyses of caries-preventive programs provide weaker evidence than do clinical trials, and results of such studies have been mixed. Reports of benefits from the use of supplements have come from Britain, New Zealand, the Netherlands, and Sweden (13-17), although the bias that comes from self-selection of supplement users was evident in all

of them. The British study, for example, reported a 61 percent reduction in DFS scores over six years; however, two-thirds of the original supplement users dropped out and numerous organizational problems were listed (13). Those who still remained in the project after six years were the most dentally conscious participants. Another illustration of selection bias comes from a South Australian report, where dental examinations of some 5,000 kindergarten children found a higher proportion of caries-free children among those who took fluoride supplements regularly than among children who lived in fluoridated areas. But those who took the tablets regularly represented only 17 percent of the children who reported taking any tablets and clearly were a select group (18). Other evaluation studies found no difference in caries experience between those children who reported using fluoride supplements and those who did not (19-23).

Two clinical trials reported since 1990 have tested fluoride supplements in combination with other fluoride therapies in school-based studies. Driscoll and colleagues (24) found that fluoride supplements, used again in the swish-and-swallow procedure over eight years, gave slightly better results than fluoride mouthrinsing; however, caries increments in all study groups were small. In Scotland, no difference in caries incidence could be found over six years between three groups of children using fluoride supplements, mouthrinse, and combinations of both with placebos (25). The Glasgow researchers speculated that since the fluoride mouthrinsing was supervised, the most likely explanation for the poor performance of the fluoride supplements was that the children either were not receiving them or they were being used incorrectly. A Swedish study comparing supplements, fluoride toothpaste, and fluoride varnish could find no difference in caries experience among the groups (26).

Evidence for the efficacy of any preventive procedure needs to come, as far as possible, from clinical trials that meet specific criteria for quality. Where fluoride supplements are concerned, only a handful of trials meet these standards. The evidence from these trials is favorable, and is all from studies conducted with school-aged

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It is concluded from these studies that while some preeruptive benefits are possible, the evidence for the efficacy of fluoride supplements when ingested from birth or early infancy is hardly strong enough to offset the disadvantages of such usage.

Supplements as a Risk Factor for Fluorosis

Consistent evidence now is available from both human and animal studies that the critical period for the development of fluorosis is the late secretion-early maturation period of preeruptive dental enamel formation (27-29). The case-control study of Pendrys and Katz (30) provided strong evidence that fluoride supplements, when ingested prior to tooth eruption, are a risk factor for dental fluorosis.

Among earlier studies, Margolis and colleagues (7) stated that fluorosis was not found in the primary dentition; however, they did not mention fluorosis in the permanent dentition. Hennon and colleagues (31) tested fluoride-vitamin drops among infants living in areas with 0.6 to 0.8 mg/L fluoride in the drinking water and reported that no "clinically significant amounts of fluorosis" were found in any group. The data from this study, however, clearly show that fluorosis developed in the test group, whether or not it was "clinically significant." In more recent reports, Bagramian and colleagues (19) did not relate fluorosis to either supplement use or caries experience, and the Glasgow group (32) did not record any difference in fluorosis prevalence between children who began taking supplements at birth and those who started at 7 years of age. The fluorosis found among the 322 children in this study was attributed to the swallowing of fluoride toothpaste rather than to the supplements.

A substantial literature, however, associates fluorosis with supplement use (6,14,15,21-23,33-38), and a number of case studies also have been reported on fluorosis among patients who ingested 0.5 mg or 1.0 mg fluoride supplements daily from infancy (39-41). It can be concluded that fluoride supplements are a risk factor for fluorosis, especially when ingested

during the critical period of late secretion-early maturation of enamel development.

Preeruptive and Posteruptive Effects

When fluoride supplements began to be used in the 1940s, few questioned the primacy of fluoride's preeruptive effects. Most likely this assumption came from the initial investigations of fluorosis in Dean's time; because fluorosis was essentially a preeruptive condition, it was natural to assume an important role for fluoride's preeruptive caries inhibitory effects. Some benefits from posteruptive fluoride exposure were recognized in early studies (42-49); nevertheless, the assumption persisted that preeruptive effects were the primary mechanism through which fluoride exerted its benefits. Posteruptive effects also were reported from one of the first supplement studies (50), and an evaluation of fluoride tablets' effects in a large school-based program in Switzerland found clear posteruptive effects, but no preeruptive effects (51). The recommendation from these Swiss data was that fluoride tablets should be kept in the mouth for as long as possible. Driscoll's comprehensive 1974 review at the Baltimore workshop (52) included a detailed discussion of the likely contributions from supplements toward pre- and posteruptive effects. The posteruptive effects of fluoride were well recognized, although preeruptive effects were given equal weight.

The view that fluoride needed to be ingested from birth onwards for full benefits is evident from the design of the Grand Rapids fluoridation study. Data from Grand Rapids showed that the cohort born at the time fluoridation began had lower caries experience than cohorts born before fluoridation (53,54). These data have been quoted frequently to support the argument for preeruptive effects of fluoride (55); however, the argument is incomplete because the Grand Rapids study was not designed to follow cohorts born after fluoridation began. The last cohort to be followed in Grand Rapids comprised those children born in the year fluoridation began, on the assumption that anti-caries benefits would be maximized in this group (56). If caries-preventive benefits were really maximized in the cohort born when fluoridation began, then it fol-

lows that caries experience in subsequent cohorts would not drop further as a result of water fluoridation alone. But data from other naturally fluoridated areas show that caries experience continues to drop in successive cohorts, and that this phenomenon was recognizable even before fluoride toothpaste came into widespread use (57). This finding suggests that the cariostatic benefit of continuous exposure to fluoride in a community is cumulative, meaning that fluoride has its effect by means other than preeruptive incorporation into the hydroxyapatite crystal. The lack of difference in enamel fluoride content between children in the study and control groups in the Wayne County study (9) also suggested that "fluoride can restrict caries by some mechanism other than fluoride uptake in enamel" (58). The proceedings from the 1989 Georgia conference on fluoride's mechanisms of action [J Dent Res 1990;69(Spec Iss)] confirmed the primacy of the posteruptive action of fluoride.

Another report frequently quoted to support the preeruptive effect of fluoride is that of Groeneveld and colleagues (59), who use data from the Tiel-Culemborg study in the Netherlands. This thoughtful analysis continues the thinking of the Dutch group that preeruptive fluoride has its main effects on caries reduction in pit-and-fissure surfaces; however, there are problems from confounding by fluoride toothpaste in the later years of the study. A more intractable problem in any such study is how to distinguish between true preeruptive effects and the effect of a tooth erupting into a mouth where fluoride is constantly present. Whether caries develops or not in an occlusal surface is highly dependent on the oral environment during the immediate posteruptive enamel maturation period, and the maintenance of intraoral fluoride at this time is a major factor in caries prevention (60).

The Case for Eliminating Supplements for Infants and Young Children

The case is essentially a risk-benefit issue—fluoride has little preeruptive impact on caries prevention, but presents a clear risk of fluorosis. Fluoride supplements, when ingested for a preeruptive effect by infants and

young children in the United States, therefore carry more risk than benefit.

It is true that the bulk of the fluorosis seen when young children use supplements is of the mildest varieties. Statements have been made that this level of fluorosis is not "clinically significant," or is actually esthetic, or is of no public health significance. These arguments date back to Dean's development of the Community Fluorosis Index (CFI), and his view that a CFI below 0.6 did not constitute a public health problem (61). This personal view of Dean's (which he only expressed in a footnote and therefore may not have taken all that seriously) may have been correct in the depths of the Great Depression, when social deprivation and severe caries were common, but it is unlikely to be appropriate today, and it can be dangerous for dental professionals to make judgments as to what is or is not esthetic. We live in an age of high esthetic sensibilities, and evidence now is available that the public may be more aware of even mild fluorosis than had previously been imagined (32,62). This awareness should warn us that policies should be framed to keep fluorosis to a minimum if all fluoride use is not to be jeopardized.

The amount of fluoride in early childhood that would lead to fluorosis was originally estimated by Forsman (63) to be 0.1 mg F/kg body weight/day. Since then this estimate has been revised downward to a range of 0.03 to 0.1 mg F/kg body weight/day (64), with reports that intakes at the lower end of this range can cause a "surprisingly high" severity of fluorosis in Kenyan children (65). There was a time when the ingestion of fluoride in the range of 0.05 to 0.07 mg F/kg body weight/day was considered "optimal" for preeruptive caries prevention (66). In light of present knowledge that preeruptive fluoride has little preventive effect, this range has better application as an estimate of the maximum amount to be ingested by young children if fluorosis is to be kept at its lowest level.

One estimate of a "safe" level is that a daily intake of 0.25 mg fluoride from birth is not associated with fluorosis (67), although the authors did not state if they meant literally any fluorosis or the more obvious type. This statement was made to support the use of supplements from birth according to the

Glasgow schedule (32), which requires the exclusion of fluoride ingestion from all other sources. Stephen's argument that supplements at 0.25 mg daily from birth will not cause fluorosis depends on parents' not using fluoride toothpaste for their children and on there being very little fluoride in the foods and beverages ingested in a normal diet. But even if a supplement, as the sole source of fluoride, is "the most accurate dosage form" (67) of fluoride ingestion, many dentists cannot accept this regimen's requirement to avoid the use of fluoride toothpaste in children younger than 7 years of age. In modern North American conditions, when fluoride is being ingested from many sources (much of it inadvertent), it is likely that many young children are ingesting 0.4-0.6 mg fluoride per day from foods, beverages, and toothpaste (68). These amounts are quite enough to cause obvious fluorosis without adding more fluoride from a supplement. When the risks and benefits of fluoride supplements are being considered, total fluoride ingestion from all sources must be borne in mind.

A number of recommendations for reduced schedules for fluoride supplements have been made, including those by the European community (69) and Canada (70). Recommendations to do so have been made in Australia (71) and Switzerland (72) on the grounds made in this review, namely that the use of supplements increases the risk of fluorosis while contributing little to caries prevention. Both the European and the Canadian schedules emphasize that the supplements are for high-risk individuals only, not for public health use, and dosage in both should not commence before 3 years of age.

It is possible that supplements have a role to play in older children and adults (67); the chewing, swishing, and swallowing of a fluoride supplement once or twice per day may help in caries control of higher-risk individuals of any age, and for those older than 7 years of age the risk of fluorosis is no longer present. The intent is that the supplements will help maintain levels of fluoride in the oral cavity, a goal that is the basis of caries prevention through the use of fluoride. The beneficial use of fluoride supplements in this way still remains to be tested, and other methods exist, mostly

through fluoride in the drinking water and in toothpaste, to maintain the fluoride level in the oral cavity.

The exposure to fluoride from multiple sources, a fact of life in the United States today, is a prime reason dental caries experience has been reduced to its current low levels. The caries decline is a major public health achievement that must be preserved in those who have benefited from it, and extended to those remaining segments of society who need it most. But the role of fluorides in meeting this challenge has to be carefully thought through, and it is hard to envision the use of supplements in young children being part of it. The additional reductions in dental caries to be achieved from using fluoride supplements, on top of what we already have from fluoride in drinking water, toothpaste, professional dental products, mouthrinses, and uncontrolled amounts in foods and beverages, has to be marginal at best. On the other hand, the risk of fluorosis from the use of supplements is clear. If the public decides that it does not want dental fluorosis, however mild it may seem to us, then it is possible that all uses of fluoride could be jeopardized. We can all agree that such a tragic outcome is not worth the risk, remote though it may seem, for marginal benefits. For that reason, fluoride supplements should no longer be used for infants and young children in the United States.

References

1. Driscoll WS, Horowitz HS. A discussion of optimal dosage for dietary fluoride supplementation. *J Am Dent Assoc* 1978; 96:1050-3.
2. Driscoll WS. What we know and don't know about dietary fluoride supplements—the research basis. *J Dent Child* 1985;52:259-64.
3. American Dental Association, Council on Dental Therapeutics. Prescribing supplements of dietary fluorides. *J Am Dent Assoc* 1958;56:589-91.
4. Binder K, Driscoll WS, Schutzmannsky G. Caries-preventive fluoride tablet programs. *Caries Res* 1978;12:22-30.
5. Szpunar SM, Burt BA. Evaluation of appropriate use of dietary fluoride supplements in the US. *Community Dent Oral Epidemiol* 1992;20:148-54.
6. Aasenden R, Peebles TC. Effects of fluoride supplementation from birth on deciduous and permanent teeth. *Arch Oral Biol* 1974;19:321-6.
7. Margolis FJ, Reames HR, Freshman E, Macauley JC, Mehaffey H. Fluoride: ten-year prospective study of deciduous and permanent dentition. *Am J Dis Child* 1975;130:794-800.

8. Arnold FA Jr, McClure FJ, White CL. Sodium fluoride tablets for children. *Dent Prog* 1960;1:8-12.
9. Driscoll WS, Heifetz SB, Korts DC. Effect of chewable fluoride tablets on dental caries in schoolchildren: results after six years of use. *J Am Dent Assoc* 1978;97:820-4.
10. Driscoll WS, Heifetz SB, Brunelle JA. Caries-preventive effects of fluoride tablets in schoolchildren four years after discontinuation of treatments. *J Am Dent Assoc* 1981;103:878-81.
11. DePaola PF, Lax M. The caries-inhibiting effect of acidulated phosphate-fluoride chewable tablets: a two-year double-blind study. *J Am Dent Assoc* 1968;76:554-7.
12. Stephen KW, Campbell D. Caries reduction and cost benefit after 3 years of sucking fluoride tablets daily at school. A double-blind trial. *Br Dent J* 1978;144:202-6.
13. Allmark C, Green HP, Linney AD, Willis DJ, Picton DC. A community study of fluoride tablets for schoolchildren in Portsmouth. Results after six years. *Br Dent J* 1982;153:426-30.
14. de Liefde B, Herbison GP. The prevalence of development defects of enamel and dental caries in New Zealand children receiving differing fluoride supplementation, in 1982 and 1985. *NZ Dent J* 1989;85:2-8.
15. D'Hoore W, Van Nieuwenhuysen JP. Benefits and risks of fluoride supplementation: caries prevention versus dental fluorosis. *Eur J Pediatr* 1992;151:613-16.
16. Widenheim J, Birkhed D. Caries-preventive effect on primary and permanent teeth and cost-effectiveness of a NaF tablet preschool program. *Community Dent Oral Epidemiol* 1991;19:88-92.
17. Widenheim J, Birkhed D, Granath L, Lindgren G. Preeruptive effect of NaF tablets on caries in children from 12 to 17 years of age. *Community Dent Oral Epidemiol* 1986;14:1-4.
18. Fanning EA, Cellier KM, Somerville CM. South Australian kindergarten children: effects of fluoride tablets and fluoridated water on dental caries in primary teeth. *Aust Dent J* 1980;25:259-63.
19. Bagramian RA, Narendran S, Ward M. Relationship of dental caries and fluorosis to fluoride supplement history in a nonfluoridated sample of schoolchildren. *Adv Dent Res* 1989;3:161-7.
20. Friis-Hasche E, Bergmann J, Wenzel A, Thylstrup A, Pedersen KM, Petersen PE. Dental health status and attitudes to dental care in families participating in a Danish fluoride tablet program. *Community Dent Oral Epidemiol* 1984;12:303-7.
21. Holm AK, Andersson R. Enamel mineralization disturbances in 12-year-old children with known early exposure to fluorides. *Community Dent Oral Epidemiol* 1982;10:335-9.
22. Kalsbeek H, Verrips E, Dirks OB. Use of fluoride tablets and effect on prevalence of dental caries and dental fluorosis. *Community Dent Oral Epidemiol* 1992;20:241-5.
23. Thylstrup A, Fejerskov O, Bruun C, Kann J. Enamel changes and dental caries in 7-year-old children given fluoride tablets from shortly after birth. *Caries Res* 1979;13:265-76.
24. Driscoll WS, Nowjack-Raymer R, Selwitz RH, Li SH, Heifetz SB. A comparison of the caries-preventive effects of fluoride mouthrinsing, fluoride tablets, and both procedures combined: final results after eight years. *J Public Health Dent* 1992;52:111-16.
25. Stephen KW, Kay EJ, Tullis JI. Combined fluoride therapies. A 6-year double-blind school-based preventive dentistry study in Inverness, Scotland. *Community Dent Oral Epidemiol* 1990;18:244-8.
26. Petersson LG, Koch G, Rasmusson CG, Stanke H. Effect on caries of different fluoride prophylactic programs in pre-school children. A two-year clinical study. *Swed Dent J* 1985;9:97-104.
27. Den Besten PK, Thariani H. Biological mechanisms of fluorosis and level and timing of systemic exposure to fluoride with respect to fluorosis. *J Dent Res* 1992;71:1238-43.
28. Evans RW, Stamm JW. An epidemiologic estimate of the critical period during which human maxillary central incisors are most susceptible to fluorosis. *J Public Health Dent* 1991;51:251-9.
29. Larsen MJ, Richards A, Fejerskov O. Development of dental fluorosis according to age at start of fluoride administration. *Caries Res* 1985;19:519-27.
30. Pendrys DG, Katz RV. Risk of enamel fluorosis associated with fluoride supplementation, infant formula, and fluoride dentifrice use. *Am J Epidemiol* 1989;130:1199-208.
31. Hennon DK, Stookey GK, Beiswanger BB. Fluoride-vitamin supplements: effects on dental caries and fluorosis when used in areas with suboptimum fluoride in the water supply. *J Am Dent Assoc* 1977;95:965-71.
32. Stephen KW, McCall DR, Gilmour WH. Incisor enamel mottling prevalence in child cohorts which had or had not taken fluoride supplements from 0-12 years of age. *Proc Finn Dent Soc* 1991;87:595-605.
33. de Liefde B, Herbison GP. Prevalence of developmental defects of enamel and dental caries in New Zealand children receiving differing fluoride supplementation. *Community Dent Oral Epidemiol* 1985;13:164-7.
34. Larsen MJ, Kirkegaard E, Poulsen S, Fejerskov O. Dental fluorosis among participants in a nonsupervised fluoride tablet program. *Community Dent Oral Epidemiol* 1989;17:204-6.
35. Riordan PJ, Banks JA. Dental fluorosis and fluoride exposure in Western Australia. *J Dent Res* 1991;70:1022-8.
36. Suckling GW, Pearce EI. Developmental defects of enamel in a group of New Zealand children: their prevalence and some associated etiological factors. *Community Dent Oral Epidemiol* 1984;12:177-84.
37. Woltgens JH, Etty EJ, Nieuwland WM. Prevalence of mottled enamel in permanent dentition of children participating in a fluoride programme at the Amsterdam dental school. *J Biol Buccale* 1989;17:15-20.
38. Woolfolk MW, Faja BW, Bagramian RA. Relation of sources of systemic fluoride to prevalence of dental fluorosis. *J Public Health Dent* 1989;49:78-82.
39. Corpron RE, Burt BA. Fluorosis from supplementation with fluoride tablets: a case report. *J Mich Dent Assoc* 1978;60:615-18.
40. Messer LB, Walton JL. Fluorosis and caries experience following early postnatal fluoride supplementation: a report of 19 cases. *Pediatr Dent* 1980;2:267-74.
41. Osuji OO, Nikiforuk G. Fluoride supplement-induced dental fluorosis: case reports. *Pediatr Dent* 1988;10:48-52.
42. Hayes RL, Littleton NW, White CL. Post-eruptive effects of fluoridation on first permanent molars of children in Grand Rapids, Michigan. *Am J Public Health* 1957;47:192-9.
43. Klein H. Dental caries in relocated children exposed to water containing fluorine. I. Incidence of new caries after 2 years of exposure among previously caries-free permanent teeth. *Public Health Rep* 1945;60:1462-7.
44. Klein H. Dental caries (DMF) experience in relocated children exposed to water containing fluorine. II. *J Am Dent Assoc* 1946;33:1136-41.
45. Ast DB, Chase HC. The Newburgh-Kingston caries fluorine study. IV. Dental findings after six years of fluoridation. *Oral Surg* 1953;6:114-23.
46. Arnold FA Jr, Dean HT, Knutson JW. Effect of fluoridated public water supplies on dental caries incidence. Results of the seventh year of study at Grand Rapids and Muskegon, Michigan. *Public Health Rep* 1953;68:141-8.
47. Backer-Dirks O. The relation between the fluoridation of water and dental caries experience. *Int Dent J* 1967;17:582-605.
48. Russell AL. Dental effects of exposure to fluoride-bearing Dakota sandstone waters at various ages and for various lengths of time. II. Patterns of dental caries inhibition as related to exposure span, to elapsed time since exposure, and to periods of calcification and eruption. *J Dent Res* 1949;28:600-12.
49. Russell AL, Hamilton PM. Dental caries in permanent first molars after eight years of fluoridation. *Arch Oral Biol* 1961;6:50-7.
50. Bibby BG, Wilkins E, Witol E. A preliminary study of the effects of fluoride lozenges and pills on dental caries. *Oral Surg Oral Med Oral Pathol* 1955;8:213-16.
51. Marthaler TM. Caries inhibiting effect of fluoride tablets. *Helv Odont Acta* 1969;13:1-13.
52. Driscoll WS. Potential benefits to be derived from fluoride tablets. In: Forrester DJ, Schulz EM Jr, eds. International workshop on fluorides and dental caries reductions. Baltimore, MD: University of Maryland School of Dentistry, 1974:25-93.
53. Arnold FA Jr, Dean HT, Jay P, Knutson JW. Effect of fluoridated public water supplies on dental caries prevalence. 10th year of the Grand Rapids-Muskegon study. *Public Health Rep* 1956;71:652-8.
54. Arnold FA Jr, Likins RC, Russell AL, Scott DB. Fifteenth year of the Grand Rapids fluoridation study. *J Am Dent Assoc* 1962;65:780-5.

55. Murray JJ. Efficacy of preventive agents for dental caries. *Caries Res* 1993;27(Suppl):2-8.
56. Arnold FA Jr. Grand Rapids fluoridation study—results pertaining to the 11th year of fluoridation. *Am J Public Health* 1957;47:539-45.
57. Johnston DW, Grainger RM, Ryan RK. The decline of dental caries in Ontario schoolchildren. *J Can Dent Assoc* 1986;5:411-17.
58. Shern RJ, Driscoll WS, Korts DC. Enamel biopsy results of children receiving fluoride tablets. *J Am Dent Assoc* 1977;95:310-14.
59. Groeneveld A, Van Eck AAMJ, Backer Dirks O. Fluoride in caries prevention: is the effect pre- or posteruptive? *J Dent Res* 1990;69(Spec Iss):751-5.
60. Bruun C, Lambrou D, Larsen MJ, Fejerskov O, Thylstrup A. Fluoride in mixed human saliva after different topical fluoride treatments and possible relation to caries inhibition. *Community Dent Oral Epidemiol* 1982;10:124-9.
61. Dean HT. Epidemiological studies in the United States. In: Moulton FR, ed. *Dental caries and fluorine*. Washington, DC: American Association for the Advancement of Science, 1946:5-31.
62. Riordan PJ. Perceptions of dental fluorosis. *J Dent Res* 1993;72:1268-74.
63. Forsman B. Early supply of fluoride and enamel fluorosis. *Scand J Dent Res* 1977;85:22-30.
64. Fejerskov O, Stephen KW, Richards A, Speirs R. Combined effect of systemic and topical fluoride treatments on human deciduous teeth—case studies. *Caries Res* 1987;21:452-9.
65. Baelum V, Fejerskov O, Manji F, Larsen MJ. Daily dose of fluoride and dental fluorosis. *Tandlaegebladet* 1987;91:452-6.
66. Ophaug RH, Singer L, Harland BF. Estimated fluoride intake of average two-year-old children in four dietary regions of the United States. *J Dent Res* 1980;59:777-81.
67. Stephen KW. Systemic fluorides: drops and tablets. *Caries Res* 1993;27(Suppl 1):9-15.
68. Burt BA. The changing patterns of systemic fluoride intake. *J Dent Res* 1992;71:1228-37.
69. Clarkson J. A European view of fluoride supplementation. *Br Dent J* 1992;172:357.
70. Anonymous. Fluoride recommendations released. Canadian Conference on the Evaluation of Current Recommendations Concerning Fluorides, April 9-11, 1992. *J Can Dent Assoc* 1993;59:303, 334-6.
71. Riordan PJ. Fluoride supplements in caries prevention: a literature review and proposal for a new dosage schedule. *J Public Health Dent* 1993;53:174-89.
72. Marthaler TM. Age-adjusted limits of fluoride intake to minimize the prevalence of fluorosis. *J Biol Buccale* 1992;20:121-7.

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