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Current and future role of fluoride in nutrition

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It is almost universally known and accepted by all reputable health organizations that fluoride is effective in preventing one of the most common of human diseases: dental caries. Although the actual substance was unknown to him at the time, McKay [1], in the early 1900s, was the first to note the caries-preventive effects of a presumably water-borne substance. Subsequently, the substance in the water supply with caries-preventive properties was identified as fluoride, and further research by Dean et al [2,3] established 1.0 parts per million (ppm) as the optimal water fluoride concentration. In 1945, fluoride was added to the water supply of Grand Rapids, Michigan for the express purpose of caries prevention and, since that time, fluoridation has become widespread in North America.

It was once believed that fluoride primarily was effective in caries prevention through systemic ingestion during tooth development, and fluoridated water and dietary fluoride supplements were developed to accommodate this mechanism of action [4]. Current evidence strongly suggests that fluorides work primarily by topical means through direct action on the teeth and dental plaque [4]. Thus, ingestion of fluoride is not essential for caries prevention, although as discussed below, water fluoridation and dietary supplements have been found to be very effective in caries prevention. In addition, some ingestion is inevitable with topical agents (such as dentifrice) and, due to a number of factors, there are many sources of fluoride in the diet. Moreover, there are consequences to excessive fluoride ingestion. Therefore, it is important to monitor fluoride as a component in the diet and as part of human nutrition.

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This article reviews therapeutic fluorides, sources of fluoride in the diet, fluoride content of foods and beverages, daily fluoride ingestion, and fluoride toxicity.

Therapeutic fluorides

Water fluoridation

In the United States, about 66% of the United States population on public water systems receives fluoridated tap water (about 58% of the total population) [5], whereas in Canada, about 40% receive optimally fluoridated tap water [6]. In addition, most of the largest United States cities are optimally fluoridated [7].

"Optimal" water fluoride concentrations that minimize the risk for both dental fluorosis and dental caries vary between 0.7 ppm and 1.2 ppm, depending on mean temperature. This variation in concentration is based on the presumption that people in cold climates consume less water, on average, than do people in warmer climates [8]. Thus, water systems in colder climates are recommended to have higher fluoride levels than those in warmer areas [9]. This assumption, based on limited studies from nearly 50 years ago, has recently been called into question [10].

Water sources, including private wells, vary greatly in fluoride content, which can range from less than 0.1 ppm to 8.0 ppm or higher [11]. In the United States, the Environmental Protection Agency has set the maximum contaminant level for fluoride at 4.0 ppm for drinking water [9]. Under this legislation (the Primary Drinking Water Standards), municipalities are required to remove fluoride when concentrations exceed 4.0 ppm fluoride [9]. The Environmental Protection Agency recommends fluoride concentrations not exceed 2.0 ppm, but this standard is not an enforceable one, so municipalities are not compelled by force of federal law to remove fluoride when concentrations are less than 4.0 ppm [9,12]. In the United States, therefore, most tap water sources contain less than 2.0 ppm fluoride, with a few municipalities containing between 2.0 ppm and 4.0 ppm fluoride and some private wells in excess of 4.0 ppm fluoride.

Although tap water sources coming into homes and businesses are regulated to some degree and fluoride levels are monitored, many individuals consume water other than from their home tap water [13]. Although water-softening systems do not remove fluoride, some water filtration systems can remove it. For example, water filtration devices based on activated charcoal remove little, if any, fluoride, whereas more expensive reverse osmosis or distillation systems remove in excess of 90% of the fluoride [14–16]. In addition, many individuals consume most of their water at work or school, sites that may have very different fluoride concentrations from their home tap water [13].

Bottled waters have become increasingly popular in the United States and Canada in recent years, with most bottled water containing less than 0.4 ppm fluoride. There can be considerable variation, however, in fluoride concentrations among bottled waters. For example, one study found that 83% of bottled waters sold in Iowa contained <0.3 ppm fluoride, with 10% having fluoride concentrations of 0.7 ppm or greater [17]. An earlier Iowa study found that 9 of 12 bottled waters tested contained 0.3 ppm or less fluoride and only one sample contained as much as 1.0 ppm [18]. Nowak and Nowak [15] found that only 1 of 19 bottled water samples from Iowa had fluoride concentrations of 0.75 ppm or higher, with the other 18 having fluoride concentrations of 0.33 ppm or lower [14]. A study of bottled waters in Texas found that 34 of 39 waters tested had fluoride concentrations of 0.30 ppm or less [16]. An earlier Texas study of bottled water fluoride concentrations found no water with greater fluoride concentration than 0.79 ppm, with most bottled waters containing less than 0.30 ppm [19]. A study of bottled waters used in Colorado found that most were low in fluoride, but bottled waters with artesian well sources consistently had fluoride concentrations of 1.20 ppm or higher [20]. Bottled waters purchased in the greater Boston area were also found to be low in fluoride concentration, with 14 of 24 products containing 0.30 ppm or less, and only 4 products containing 0.7 ppm fluoride or higher [21].

Thus, fluoride ingestion from water can vary greatly for individuals over time and from individual to individual because of differences in water consumption, fluoride concentrations, filtration systems, and bottled water use. For this reason, it is important that individual water sources be tested for fluoride content before prescribing or recommending fluoride products for young children (such as fluoride supplements) in order to limit their fluoride ingestion.

Effectiveness of water fluoridation in caries prevention

There is overwhelming evidence that fluorides prevent dental caries in both children and adults. The specific effectiveness attributable to water fluoridation in caries prevention appears to be inversely related to the number of other available fluoride exposures (eg, fluoride dentifrice). Thus, early United States studies of the effectiveness of water fluoridation, conducted before the advent of fluoride dentifrice and other sources of fluoride, found that reductions in caries were on the order of 50% to 70% for permanent teeth and 40% to 60% for primary teeth [13,22]. With more widespread availability of fluorides from other sources, the effectiveness attributable specifically to water fluoridation is less, so that more recent estimates of water fluoridation effectiveness are in the range of 20% to 30% [22–24].

Recent studies from outside North America are noteworthy in their assessments of the effectiveness of water fluoridation. For example, a study of caries in the primary dentition in fluoridated and nonfluoridated communities in the United Kingdom found a significantly higher proportion of caries-free children in the fluoridated communities [25]. In contrast, a study of a community that discontinued water fluoridation found no increases in caries prevalence after 3 years and no significant differences in caries prevalence between the previously fluoridated community and a similar community that was never fluoridated [26]. It should be noted, however, that individuals from both communities in the study received intensive topical fluoride therapies including frequent fluoride varnish applications that may have masked the benefits of fluoridation. Perhaps more enlightening was a study of water fluoridation, caries, and socioeconomic status (SES) in 12-year-old United Kingdom children [27]. This study found that water fluoridation was more effective in caries prevention among children from lower SES families and that among children from "average" SES families, there was 37% less decay experience among those in fluoridated areas compared with those from nonfluoridated areas [27].

Taken together, there is substantial evidence supporting the effectiveness of water fluoridation in caries prevention. It is also clear, however, that the effectiveness of water fluoridation is greatest in the absence of other fluoride sources. Thus, although some would argue that water fluoridation is unnecessary in light of the widespread availability of other fluorides, evidence suggests that water fluoridation remains a very effective, economical means of caries prevention [23].

Opposition to water fluoridation

As described by Newbrun [28], individuals opposed to water fluoridation "are a heterogeneous lot," and they have used a variety of strategies to argue against water fluoridation. Their arguments can be grouped into four broad categories: (1) fluoridation is harmful to health, (2) fluoridation is expensive and not effective, (3) fluoridation is an insult to the environment and pollutes the "purity" of water, and (4) fluoridation infringes on individuals' free choice. Each of these areas is discussed individually below [28,29].

Antifluoridationists have implicated fluorides, specifically water fluoridation, as causing a variety of diseases and conditions. These have included cancer, birth defects, osteoporosis, AIDS, infertility, general mortality, and numerous other diseases and conditions [29]. In making such arguments, the antifluoridationists often cite poorly conducted or poorly controlled studies, studies conducted with insects or animals, or anecdotal "evidence" but can often make convincing arguments to lay audiences. For example, in an oft-cited study that compared death rates among life-long residents of two small Texas towns with vastly different water fluoride concentrations (8.0 ppm and 0.4 ppm), antifluoridationists reported 14 deaths in the high-fluoride community compared with only 4 deaths in the low-fluoride community over a 10-year period [28]. The antifluoridationists, however, failed to point out that the population was much older, on average, in the high-fluoride community, a factor that would easily explain the differences in the respective death rates. As in the above example, rigorous scientific reviews of the studies cited by the antifluoridationists have found absolutely no evidence to support claims that fluoridation poses a serious health risk [13,28].

The overwhelming evidence demonstrating the effectiveness of fluoridation has effectively refuted claims that fluoridation is not effective or overly expensive, and numerous analyses have confirmed the cost effectiveness of fluoridation [13,23]. For example, a recent analysis of fluoridation confirmed its cost effectiveness while allowing for other fluoride exposures [23], and the United States Centers for Disease Control and Prevention recently listed water fluoridation as among the top ten public health measures of the twentieth century [30] and strongly recommends its use [31].

Similarly, antifluoridationists' claims that fluoridation is unnatural and pollutes the environment have been refuted by the fact that virtually all water supplies have detectable levels of naturally occurring water fluoride, with many communities having naturally occurring fluoride concentrations in the optimal range of 0.7 ppm to 1.2 ppm. In addition, fluoride is but one of many chemicals added to water supplies so that few, if any, sources dispense "pure" water, yet there is little concern about the addition of chemicals other than fluoride [28].

Perhaps the antifluoridationists' strongest argument is that by adding fluoride to public water systems, some individuals who do not desire fluoridated water receive it against their will, thus depriving them of their freedom of choice. Again, however, there is little opposition to other chemicals added to public water supplies, and numerous United States courts have upheld the constitutionality of fluoridation [4,28].

In summary, although antifluoridationists have made numerous arguments against water fluoridation, to date, none of their claims have demonstrated any notable scientific merit, and higher courts have not supported any of their legal arguments.

Dietary fluoride supplements

Dietary fluoride supplements were developed in the 1940s to take the place of water fluoridation for those in nonfluoridated areas. Early studies suggested that supplements were equally effective as water fluoridation in caries prevention because several studies reported caries reductions of 50% to 80% [4]. Most of these studies, however, had methodological flaws, and more reasonable estimates of the caries-preventive effect of dietary fluoride supplements are in the range of 20% to 30% [4]. Dietary fluoride supplements are usually dispensed in the form of drops for infants and as chewable tablets or lozenges for older children. In the United States, dosages range from 0.25 mg to 1.0 mg F, per day, according to age and the fluoride concentration of the patient's predominant drinking water source (Table 1)

Table 1
Recommended dietary fluoride supplement dosage (mg F/d)

	Water fluoride concentration (ppm)		
Age	<0.3	0.3–0.6	>0.6
Birth–6 mo	—	—	—
6 mo–3 y	0.25	—	—
3–6 y	0.50	0.25	—
>6 y	1.00	0.50	—

From American Dental Association, Council on Dental Therapeutics. New Fluoride schedule adopted: therapeutics council affirms workshop outcome. ADA News 1994;25:12–14.

[14,32]. In Canada, supplement recommendations are more conservative, with supplements recommended only for high-risk children and only after the eruption of the first permanent tooth, when the risk for developing dental fluorosis is reduced [33].

Compliance with fluoride supplements is often low, so that many children appropriately prescribed supplements do not receive them on the prescribed, daily basis [34,35]. On the other hand, several studies have found that physicians and dentists often prescribe supplements inappropriately, such as when supplements are prescribed for children residing in optimally fluoridated communities [36,37]. Thus, there can be considerable variation in fluoride intake from the use of supplements because of variability in compliance and prescribing patterns. The use of fluoride supplements has frequently been identified as a risk factor for dental fluorosis. Because supplements can be a significant source of ingested fluoride for children receiving them [38–48], supplements should be targeted at children at high risk for dental caries [31,33].

Fluoridated salt

Fluoridated salt was developed as an alternative to water fluoridation for areas where water fluoridation was either politically untenable or technically impractical. Thus, fluoridated salt is most widely used in central Europe and in Central and South America. Salt fluoridation involves the addition of potassium fluoride to table salt at a concentration of 250 mg to 350 mg potassium fluoride per kilogram of salt [4].

There have been only limited studies of the effectiveness of salt fluoridation in caries prevention but they have consistently shown that it is effective [49–52]. For example, a cross-sectional study in Strasbourg, France, demonstrated that children using fluoridated salt had decayed or filled primary teeth (dft) values 35% lower, on average, than those using nonfluoridated salt [50]. This difference was statistically significant, although a difference of similar magnitude in decayed, missing or filled permanent tooth surfaces (DMFS) was not [20]. Two repeat cross-sectional studies comparing caries prevalence in children of the same age groups before and after initiation of salt fluoridation were conducted in Jamaica and Mexico [49,51]. In both studies, dramatic reductions in caries prevalence and severity were observed following the initiation of salt fluoridation [49,51]. As with any study that compares findings across time, however, the reductions in caries experience cannot be directly attributed to salt fluoridation alone because other factors (such as changes in use of other fluorides) may have played a role. It should also be noted that as a practical matter, salt fluoridation projects have been limited to relatively small geographic areas where food distribution systems are relatively simple. It has been suggested that salt fluoridation in the United States and Canada may not be practical due to the complexities of the food distribution systems, the numerous salt processors and distributors, and the relative ease of fluoridating water supplies [4].

Fluoridated milk

Similar to salt fluoridation, milk fluoridation was developed as an alternative to water fluoridation, although relatively few studies have effectively assessed its effectiveness in caries prevention. Some studies from the 1960s and 1970s suggested that milk fluoridation was very effective in caries prevention; however, because these studies had serious methodological concerns, milk fluoridation's effectiveness could not be accurately assessed [53]. Since that time, Stephen et al [54] reported, in a double-blind study, that after 5 years, milk fluoridation resulted in a 48% reduction in DMFS for a group of children drinking fluoridated milk (mean DMFS = 3.29) compared with a control group (mean DMFS = 6.33). A study in Bulgaria found that milk fluoridation reduced DMFS by 30% to 85%, depending on the age of the children at the time of milk fluoridation [55]. This latter study, however, was a repeat cross-sectional study and not a longitudinal one, so it is difficult to attribute caries prevention entirely to milk fluoridation. It should be noted that there are many potential obstacles to initiating milk fluoridation, including logistical, financial, and legal ones, so that it remains to be seen as to whether milk fluoridation will ever become a widespread means of caries prevention [56].

Other therapeutic fluorides

There are a number of therapeutic fluoride products that may contribute fluoride to the diet. These include dentifrice, with typical fluoride concentrations of 1000 ppm to 1100 ppm, over-the-counter 0.05% sodium fluoride mouth rinses that contain 230 ppm fluoride, prescription 0.20% sodium fluoride rinses that contain 920 ppm, and prescription fluoride gels that contain 1000 ppm to 5000 ppm [57]. Although none of these products are meant to be ingested, young children are often not capable of expectorating and, thus, may ingest significant amounts of fluorides from these products.

Because about 95% of all toothpaste sold in the United States and Canada contains fluoride [57–59], dentifrice is a widely available source of fluoride. Because of its ubiquity and relatively high fluoride concentration, it can be a significant source of fluoride in the diet, particularly among younger children. As reviewed by Levy [60], there is a great deal of variability in the use of fluoride dentifrice among individual children in terms of amounts used, amounts ingested, and the age at which children begin to use it. Based on previous studies, the review concluded that among 2-year-olds and 3-year-olds, mean daily fluoride ingested from dentifrice was about 0.3 g, or about two thirds of the amount of dentifrice placed on the toothbrush, but that there was a great deal of variability in amounts ingested [60].

Because of their high fluoride concentrations, professionally applied fluoride therapies such as fluoride varnish (22,000 ppm) and office topical gels and foams (9,000–12,300 ppm), can be potential sources of large amounts of ingested fluoride, although they are typically used only on a semiannual basis [4]. Thus, use of such products should be done with caution for patients (such as young children), for whom acute fluoride toxicity is a consideration. In particular, due to the amount of product used, office topical gels and foams should be avoided in younger children to avoid acute toxicity (discussed later in this article) except in patients with a high risk for caries and a clear need for aggressive caries prevention.

Sources of fluoride in the diet

Foods and beverages can be sources of substantial amounts of fluoride in the diet. Some of the fluoride in the diet can be attributed to the so-called "halo effect" or "diffusion effect," whereby persons not residing in fluoridated communities who consume products from fluoridated communities receive some of the benefits of fluoridation [13]. In this way, fluoride from fluoridated water becomes incorporated into products containing water or products that are processed with water. In addition, specific foods and beverages have relatively high fluoride concentrations due to a variety of natural and food-processing factors. Thus, a variety of foods and beverages can contribute fluoride to the diet.

Fluoride content of foods and beverages

Fluoride content of foods

The fluoride concentration of foods has not been widely reported, but it appears that most foods that are found to have relatively high fluoride concentrations generally are not inherently rich in fluoride. Instead, their high fluoride concentrations are typically the result of specific manufacturing processes. For example, certain processed chicken products have been found in separate studies to have fluoride concentrations of 4.4 ppm [61] and 10.0 ppm [62] due to the mechanical deboning process whereby bone fragments high in fluoride are mixed with the meat. Similarly, although seafood often contains moderate levels of fluoride [63], drying seafood concentrates the fluoride; one study reported the fluoride concentration of dried fish and seafood to be as high as 40.0 ppm [64].

The majority of foods assessed for fluoride are those meant for infants and young children. As with chicken and seafood, food processing often concentrates fluoride, and foods processed with fluoridated water typically have higher fluoride concentrations than foods processed with nonfluoridated water. The method and site of processing infant cereals has been shown to affect their fluoride concentration. A study that found marked differences between cereals processed in fluoridated and nonfluoridated areas [62] showed that cereals processed in a fluoridated area had fluoride concentrations ranging from 3.8 ppm to 6.3 ppm, whereas those processed at nonfluoridated sites had fluoride concentrations of 0.9 ppm to 2.1 ppm [62]. Among other infant foods, a creamed spinach product was reported to have a fluoride concentration of 2.0 ppm [65], whereas at the other extreme, peaches and pears have been reported to have fluoride concentrations of about 0.1 ppm [62]. Most infant food products, however, fall into the range of 0.3 ppm to 0.7 ppm [62,65].

Fluoride content of beverages

Soft drinks are very popular and widely consumed beverages among adults and children in the Unites States and Canada [66]. As with food products, most studies suggest that the fluoride concentration of soft drinks depends largely on the fluoride concentration of the water used in manufacturing. A study of soft drinks manufactured in Houston, Texas, illustrated this observation [67]. At the time of the study, Houston had numerous bottling plants throughout the city, and water fluoride levels varied in different parts of the city. The study found that soft-drink fluoride concentrations closely matched the fluoride concentrations of the bottling plants' water supplies and varied from 0.03 ppm to 1.55 ppm [67]. This observation was also made in other studies [68–71], which generally found that the fluoride concentrations in soft drinks were slightly less than the water fluoride concentrations of the manufacturing plants where the beverages were bottled. An important observation from one study was that soft-drink manufacturing and distribution is very complex, in that the same brand and flavor of soft drink sold in a given location may be manufactured at many different sites, depending on the size and type of container and type of packaging [68]. Often, different manufacturing sites have different water fluoride concentrations, resulting in different fluoride concentrations of the soft drink [68].

Tea and coffee are popular beverages in the United States, Canada, and throughout the world. Although coffee itself contains little fluoride (the fluoride content of brewed coffee is almost entirely dependent on the fluoride concentration of the water source used in brewing), teas have naturally high fluoride concentrations [66,70,72,73]. Mean fluoride concentrations among regular teas have been found to range from 1.33 ppm [66] to 2.56 ppm [70]. Decaffeinated teas have been reported to have significantly higher fluoride concentrations than regular teas [72] (3.19 ppm for decaffeinated tea compared with 1.50 ppm for regular tea). In contrast to regular and decaffeinated teas, herbal teas have been reported to have very low fluoride concentrations of less than 0.10 ppm [72].

Fruit juices, juice drinks, and fruit-flavored drinks are also popular beverages, especially among infants and children. As with soft drinks, the fluoride content of juice and juice-flavored products varies with differences in water fluoride concentrations at the processing sites [62,74]. Also, similar to soft drinks, there may be considerable variation in the fluoride concentrations of fruit juices and juice drinks within the same type, brand, and flavor of product, dependent on the site of manufacture. For example, an Iowa study found that a particular brand of apple juice processed at a nonfluoridated site was found to have a fluoride concentration of less than 0.1 ppm, whereas the exact same brand manufactured with fluoridated water had a fluoride concentration of 0.57 ppm [74]. The same study found that grape juices, particularly white grape juices, had elevated levels of fluoride compared with other juices and juice products [74]. The mean fluoride concentration for white grape juice was 1.33 ppm, whereas for other grape juices, the mean fluoride level was 1.00 ppm [74]. For specific juices or juice drinks, the highest fluoride concentration was 2.80 ppm for a white grape juice, whereas some brands of orange juice had fluoride concentrations of less than 0.10 ppm [74]. Other studies found wider ranges of fluoride concentrations in juices and juice products, with some white grape juices having fluoride concentrations over 4 ppm [70,75]. For example, Pang et al [70] found that the fluoride concentrations ranged from 0.01 ppm to 6.70 ppm for juices and juice drinks in North Carolina. Similarly, Stannard et al [75] found the range of fluoride concentrations was 0.15 ppm to 6.80 ppm among 43 juices and juice products in the Boston area. Overall in these studies, about 20% to 40% of juices and juice drinks tested had fluoride concentrations of 1.0 ppm or greater, whereas about half had fluoride concentrations of 0.30 ppm or less [70,74,75].

Infant formulas can be a potentially important source of fluoride in very young children. Infant formulas are sold as either "ready to feed" or as a concentrate that is mixed with water. Formula concentrates mixed with fluoridated water may be an especially significant source of ingested fluoride because formula is often the only constituent of an infant's diet, and infants may ingest 1 L/day or more of infant formula [17,34,76]. Prior to 1979, there was a great deal of variation in fluoride concentration among brands of infant formula in the United States, with some ready-to-feed infant formulas exceeding 0.7 ppm fluoride and many formulas with fluoride levels of 0.4 ppm to 0.5 ppm [62,76]. Manufacturers in the United States voluntarily reduced the fluoride concentrations of infant formulas beginning in 1979

[34,77], whereas in Canada, infant formula makers delayed reductions in fluoride content [34,78]. Even with the voluntary reductions in fluoride concentrations to levels of about 0.15 ppm to 0.30 ppm for most ready-to-feed formulas [17,77,79], these sources sometimes contribute substantially to infants' fluoride intake. Soy-based infant formulas generally have been found to have higher fluoride concentrations than do milk-based products [78]. Lastly, cow's milk and human breast milk have very low fluoride concentrations of about 0.04 ppm and 0.01 ppm, respectively [17,76,80].

Fluoride concentrations of infant formula were documented by a recent study in Iowa that reported on 33 brands of infant formulas [17]. These included ready-to-feed formulas and liquid and powder concentrates. The mean fluoride concentrations ranged from 0.12 ppm for milk-based liquid formula concentrates mixed with deionized water to 0.30 ppm for soy-based ready-to-feed formulas [17]. Higher fluoride concentrations are obtained when concentrates are mixed with optimally fluoridated water, so that fluoride concentrations can range up to 1.0 ppm for powder concentrates and 0.5 ppm for liquid concentrates [14,17].

Daily fluoride ingestion

There is no specific nutritional requirement for fluoride, and fluoride is recommended in the diet solely as a means of caries prevention [63]. Thus, the so-called "adequate intake" level is "based on estimated intakes that have been shown to reduce the occurrence of dental caries" [63]. The adequate intake levels of fluoride are 0.01 mg/day for infants up to 6 months of age, 0.5 mg/day for children 7 to 12 months of age, 0.7 mg/day for 1-year-old to 3-year-old children, 1.0 mg/day for 4-year-old to 8-year-old children, 2.0 mg/day for 9-year-old to 13-year-old children, 3.0 mg/day for females 14 years and older and males 14 to 18 years old, and 4.0 mg/day for males 19 years and older [63]. These adequate intake levels generally parallel the "optimal" fluoride intake range of 0.05 to 0.07 mg fluoride per kilogram body weight, first described by McClure in the early 1940s [12].

As described previously [81], a number of studies have attempted to estimate the mean daily fluoride ingestion of children and young adults using a variety of techniques. Such estimates of fluoride intake are inherently difficult given the great deal of variation that exists, not only in individual consumption patterns but also in the fluoride concentrations of various foods and beverages as described previously [81]. In general, studies and reviews [14,34,60] of total fluoride intake from diet and dentifrice [12,35,62,65,69,71,82–90] suggest that mean intake levels for children fall just short of meeting the adequate intake levels for fluoride. Several studies, however, suggested that children residing in fluoridated communities have higher mean fluoride intakes than those in nonfluoridated areas [82,83, 86,87] and, in at least one study, the mean for those in fluoridated areas may have exceeded the adequate intake level [89]. Given the increased prevalence of fluorosis (discussed later), it may be necessary to revise downward the adequate intake levels for fluoride. Unfortunately, because there are no studies that have specifically linked amounts of ingested fluoride from all sources to fluorosis occurrence, further research is needed before definitive recommendations can be made.

Fluoride toxicity

Chronic toxicity—skeletal and dental fluorosis

Chronic overingestion of fluoride can result in two distinct types of fluorosis: skeletal fluorosis and dental fluorosis. Skeletal fluorosis is characterized by joint stiffness and osteosclerosis in milder forms, whereas more severe skeletal fluorosis can include calcification of ligaments, muscle wasting, osteoporosis, and neurologic deficits [63]. The severity of the disease appears to be directly related to the magnitude and duration of high-fluoride exposure [63]. At low levels of chronic exposure such as with optimally fluoridated water, fluoride appears to slightly increase trabecular bone mass but has little effect on cortical bone [91–93] and little effect on overall skeletal health. It has been estimated that skeletal fluorosis begins to become symptomatic after about 10 years of fluoride exposure of at least 10 mg/day [63]. A case has also been reported where skeletal fluorosis occurred after 6 years of 50 mg/day fluoride exposure [63]. Skeletal fluorosis is very rare, with only five cases reported in the United States since the early 1960s [63].

Dental fluorosis is a much more common condition than skeletal fluorosis and is characterized by diffuse opacities on the enamel surfaces of the teeth. Dental fluorosis can occur in the primary dentition [94] and in the permanent dentition but is much more common in the permanent dentition where it is generally more noteworthy because of cosmetic concern [94]. In the permanent teeth, the diffuse opacities follow the perikymata—the developmental lines that horizontally cross the enamel surface—and may be associated with increased porosity [63]. In more severe cases, the porosity may become stained or coalesce into discrete pits. Figs. 1 and 2 represent examples of moderate fluorosis and severe fluorosis, respectfully. Dental fluorosis occurs as a result of high fluoride ingestion early in life, primarily during the maturation phases of enamel development [95–98]. The amount of daily fluoride ingestion required to produce detectable fluorosis, the duration of such exposure required to produce it, and the precise time when specific teeth are most susceptible, however, remains in question and has been the subject of intensive study [39,95,96,99–102].

There is compelling evidence that the prevalence of dental fluorosis has increased in the United States and Canada in recent years [97,103–105], particularly in nonfluoridated communities [38,97,103,105,106]. Fluorosis prevalence is generally higher in fluoridated communities [103,107] as

Fig. 1. An image of moderate fluorosis for a patient in the mixed dentition. Note the irregular areas of opaque, white enamel on the maxillary central incisors, and the characteristic white striations present near the incisal edges of the lateral incisors.

evidenced by analysis of national data in the United States where dental fluorosis prevalence was 46.4% among children with lifelong exposure to optimally fluoridated water or water with higher-than-optimal fluoride levels compared with 16.1% for children with no exposure to water fluoridation [107]. Recently, Beltrán-Aguilar et al [103] described fluorosis prevalence changes between the time of Dean's work [2,3] in the 1930s and more recent data from the late 1980s. In these analyses, the authors confirmed that prevalence had increased most in areas of low water fluoride concentrations [103]. Other studies in localized areas of the United States and Canada also have reported higher dental fluorosis prevalence in fluoridated areas than in nonfluoridated ones [108–110], as well as generally higher prevalence rates than in the United States national study [27,40,111,112].

As discussed previously, due in part to the complexity of estimating total fluoride ingestion, the amount of fluoride exposure necessary to cause dental fluorosis is largely unknown. Instead, most studies of dental fluorosis have focused on identification of risk factors. In general, studies have reported that risk factors include dietary fluoride supplements [38–48] and early use of fluoride dentifrice [41,43,45,88,95,110,111,113,114]. Other studies have also implicated prolonged use of infant formula [114] and exposure to fluoridated drinking water [111].

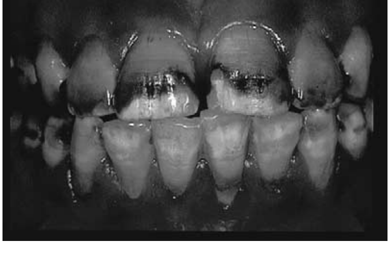

Fig. 2. A case of severe dental fluorosis. Pitting of the enamel surface and irregular areas of opaque, white enamel characterizes severe dental fluorosis. These features are often accompanied by dark (brown) staining of the enamel.

Perhaps the most important research regarding risk factors for dental fluorosis was conducted in New England by Pendrys and colleagues [42–47]. In this research (a series of case-control studies of children in fluoridated and nonfluoridated communities), risk factors for fluorosis in fluoridated communities included use of fluoride supplements [42,45,47] and powdered-concentrate infant formula [47], as well as greater frequency and amount of fluoride dentifrice used during the first 8 years of life [42,45]. In non-fluoridated areas, risk factors included early, frequent tooth brushing [46], supplement use [43,46], and high household income [43].

Acute toxicity

Acute ingestion of highly concentrated fluoride compounds can have toxic effects ranging from nausea and vomiting to death [57,115]. Younger children are most at risk for experiencing toxic effects through ingestion of large amounts of fluoride relative to body weight. There is little human data to estimate toxic doses of fluoride, but Heifetz and Horowitz [115] estimated that acute ingestion in excess of 8 mg F per kilogram body weight could result in toxic effects and that acute ingestion of 32 mg to 64 mg F per kilogram could result in death. Thus, for adults weighing 70 kg (154 pounds), death from fluoride poisoning would require ingestion of 5 g to 10 g F; for 3-year-old to 6-year-old children weighing 20 kg (44 pounds), ingestion of about 640 mg would result in death. To reach these levels of ingestion, however, large quantities of fluoride products would need to be consumed. Thus, for a child weighing 20 kg, ingestion of over 20 ounces of dentifrice (1,100 ppm), equivalent to 4 to 5 tubes of toothpaste, would be necessary to produce fatal results; however, consumption of only about 50 mL of an office topical gel (12,300 ppm) probably would be lethal in such a child. This amount is equivalent to about 3 tablespoons, so that such highly concentrated products should be used with extreme caution in preschool-aged children. It should be remembered, however, that very few deaths have been reported due to acute fluoride toxicity [4]. Some toxic effects such as nausea, vomiting, and diarrhea may occur with fluoride ingestion of about 5 mg to 8 mg per kilogram body weight [57,115]. Thus, for a toddler weighing 10 kg (22 pounds), ingestion of an ounce of dentifrice or less than 5 mL (1 teaspoon) of office topical fluoride gel may produce symptoms of toxicity.

Summary

Fluoride continues to be the cornerstone of dental caries prevention in North America and throughout the world [4], and there are a variety of sources of fluoride that may contribute to the dietary intakes of fluoride. Although the severe effect of chronic exposures to high levels of fluoride—skeletal fluorosis—is extremely rare in North America, dental fluorosis has become more prevalent [97,103–105]. To address the increase in dental fluorosis prevalence, recommendations have been made to reduce fluoride ingestion early in life [31,116]. These recommendations have included the introduction of lower concentration fluoride dentifrice for use by young children [31,112], labeling of the fluoride concentration of bottled water [31], and revised fluoride supplement guidelines to reduce or eliminate their use [31]. Because our knowledge is incomplete regarding the amount, duration, and timing of fluoride ingestion that can result in dental fluorosis, however, further research is clearly needed before definitive recommendations can be made regarding the use of fluorides, including recommended intakes of fluoride in the diet.

References

[1] McKay FS. The relation of mottled enamel to caries. J Am Dent Assoc 1928;15:1429–37.

[2] Dean HT, Arnold FA Jr, Elvove E. Domestic water and dental caries II. A study of 2,832 white children, aged 12–14 years, of eight suburban Chicago communities, including Lactobacillus acidophilus studies of 1,761 children. Public Health Rep 1941;56:761–92.

[3] Dean HT, Arnold FA Jr, Elvove E. Domestic water and dental caries V. Additional studies of the relation of fluoride domestic waters to dental caries experience in 4,425 white children, aged 12–14 years, of 13 cities in 4 states. Public Health Rep 1942;57:1155–79.

[4] Burt BA, Eklund SA. Fluoride: human health and caries prevention. In: Burt BA, Eklund SA, editors. Dentistry, dental practice and the community. 5th edition. Philadelphia: WB Saunders; 1999. p. 279–96.

[5] US Department of Health and Human Services, Centers for Disease Control and Prevention. Populations receiving optimally fluoridated public drinking water—United States, 2000. Morb Mortal Wkly Rep 2002;51:144–7.

[6] Health Canada. It's your health—fluorides and human health. Available at: http://www.hc-sc.gc.ca/english/iyh/fluorides.html, Accessed May 15, 2002.

[7] US Department of Health and Human Services, Centers for Disease Control and Prevention. Fluoridation census, 1992. Atlanta (GA): CDC; 1993.

[8] Galagan DJ, Vermillion JR. Determining optimum fluoride concentrations. Public Health Rep 1957;72:491–3.

[9] US Public Health Service. Public Health Service drinking water standards 1962. PHS Pub No. 956. Washington, DC: Government Printing Office; 1962.

[10] Sohn W, Heller KE, Burt BA. Fluid consumption related to climate among children in the United States. J Public Health Dent 2001;61:99–106.

[11] Griffin KG. Assessment of natural fluoride levels in well water with significant dental implications. Northwest Dent 1988;67:16–8.

[12] McClure FJ. Ingestion of fluoride and dental caries, quantitative relations based on food and water requirements of children 1 to 12 years old. Am J Dis Child 1943;66:362–9.

[13] Ripa LW. A half-century of community water fluoridation in the United States: review and commentary. J Public Health Dent 1993;53:17–44.

[14] Levy SM, Kiritsy MC, Warren JJ. Sources of fluoride intake in children. J Public Health Dent 1995;55:39–52.

[15] Nowak A, Nowak MV. Fluoride concentration of bottled and processed waters. Iowa Dent J 1989;75:28.

[16] Tate WH, Chan JT. Fluoride concentrations in bottled and filtered waters. Gen Dent 1994;42:362–6.

[17] Van Winkle S, Levy SM, Kiritsy MC, et al. Water and formula fluoride concentrations: significance for infants fed formula. Pediatr Dent 1995;17:305–10.

[18] McGuire S. Fluoride content of bottled water [letter]. N Engl J Med 1989;321:836.
[19] Chan JT, Stark C, Jeske AH. Fluoride content of bottled waters: implications for dietary fluoride supplementation. Tex Dent J 1990;107:17–21.
[20] Flaitz CM, Hill EM, Hicks MJ. A survey of bottled water usage by pediatric dental patients: implications for dental health. Quintessence Int 1989;20:847–52.
[21] Stannard J, Rovero J, Tsamtsouris A, Garris V. Fluoride content of some bottled waters and recommendations for fluoride supplementation. J Pedodontics 1990;14:103–7.
[22] Horowitz HS. The effectiveness of community water fluoridation in the United States. J Public Health Dent 1996;56:253–8.
[23] Griffin SO, Jones K, Tomar SL. An economic evaluation of community water fluoridation. J Public Health Dent 2001;61:78–86.
[24] O'Mullane D, Whelton HP, Costelloe P, et al. The results of water fluoridation in Ireland. J Public Health Dent 1996;56:259–64.
[25] Gray MM, Davies-Slowik J. Changes in the percentage of 5-year-old children with no experience of decay in Dudley towns since the implementation of fluoridation schemes in 1987. Br Dent J 2001;190:30–2.
[26] Seppa L, Karkkainene S, Hausen H. Caries trends 1992–1998 in two low-fluoride Finnish towns formerly with and without fluoridation. Caries Res 2000;34:462–8.
[27] Jones CM, Worthington H. Water fluoridation, poverty and tooth decay in 12-year-old children. J Dent 2000;28:389–93.
[28] Newbrun E. The fluoridation war: a scientific dispute or a religious argument. J Public Health Dent 1996;56:246–52.
[29] Yiamouyiannis J. Lifesavers guide to fluoridation. Delaware (OH): Safe Water Foundation; 1983.
[30] US Public Health Service, Centers for Disease Control and Prevention. Ten great public health achievements: United States 1900–1999. Morb Mortal Wkly Rep 1999;48:241–3.
[31] US Public Health Service, Centers for Disease Control and Prevention. Recommendations for using fluoride to prevent and control dental caries in the United States. Morb Mortal Wkly Rep 2001;50(RR14):241–2.
[32] American Dental Association, Council on Dental Therapeutics. New fluoride schedule adopted: therapeutics council affirms workshop outcome. ADA News 1994;25:12–14.
[33] Canadian Dental Association. Fluoridation—considerations re: fluoride supplementation. Available at: http://www.cda-adc.ca/public/frames/eng_index.html. Accessed May 15, 2002.
[34] Levy SM. Review of fluoride exposures and ingestion. Community Dent Oral Epidemiol 1994;22:173–80.
[35] Levy SM, Kiritsy MC, Slager SL, Warren JJ. Patterns of dietary fluoride supplement use during infancy. J Public Health Dent 1998;58:228–33.
[36] Levy SM, Carrell AF. Compliance by health care providers with recommended systemic fluoride supplementation protocol. Clin Prev Dent 1987;9:19–22.
[37] Levy SM, Muchow G. Provider compliance with recommended dietary fluoride supplement protocol. Am J Public Health 1992;82:281–3.
[38] Awad MA, Hargreaves JA, Thompson GW. Dental caries and fluorosis in 7–9 and 11–14 year old children who received fluoride supplements from birth. J Canad Dent Assoc 1994;60:318–22.
[39] Ismail AI. Fluoride supplements: current effectiveness, side effects, and recommendations. Community Dent Oral Epidemiol 1994;22:164–72.
[40] Leverett DH. Prevalence of dental fluorosis in fluoridated and nonfluoridated communities—a preliminary investigation. J Public Health Dent 1986;46:184–7.
[41] Leverett DH, Adair SM, Proskin HM. Dental fluorosis among children in fluoridated and non-fluoridated communities [abstract; special issue]. J Dent Res 1988;67:230.
[42] Pendrys DG. Risk for fluorosis in a fluoridated population. J Am Dent Assoc 1995; 126:1617–24.

[43] 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.
[44] Pendrys DG, Stamm JW. Relationship of total fluoride intake to beneficial effects and enamel fluorosis [special issue]. J Dent Res 1990;69:529–38.
[45] Pendrys DG, Katz RV, Morse DE. Risk factors for enamel fluorosis in a fluoridated population. Am J Epidemiol 1994;140:461–71.
[46] Pendrys DG, Katz RV, Morse DE. Risk factors for enamel fluorosis in a non-fluoridated community. Am J Epidemiol 1996;143:808–15.
[47] Pendrys DG, Katz RV. Risk factors for enamel fluorosis in optimally fluoridated children born after the US manufacturers' decision to reduce the fluoride concentration of infant formula. Am J Epidemiol 1998;148:967–74.
[48] 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.
[49] Esstupinan-Day SR, Baez R, Horowitz H, et al. Salt fluoridation and dental caries in Jamaica. Community Dent Oral Epidemiol 2001;29:247–52.
[50] Fabien V, Obry-Musset AM, Hedelin G, et al. Caries prevalence and salt fluoridation among 9-year-old schoolchildren in Strasbourg, France. Community Dent Oral Epidemiol 1996;24:408–11.
[51] Irigoyen ME, Sanchez-Hinojosa G. Changes in dental caries prevalence in 12-year-old students in the state of Mexico after 9 years of salt fluoridation. Caries Res 2000;34:303–7.
[52] Stephen KW, Macpherson LMD, Gorzo I, et al. Effect of fluoridated salt intake in infancy: a blind caries and fluorosis study in 8th grade Hungarian pupils. Community Dent Oral Epidemiol 1999;27:210–15.
[53] Kunzler W. Systemic use of fluoride—other methods: salt, sugar, milk, etc. Caries Res 1993;27(Suppl 1):16–22.
[54] Stephen KW, Boyle IT, Campbell D, et al. Five-year double-blind fluoridated milk study in Scotland. Community Dent Oral Epidemiol 1984;12:223–9.
[55] Pakhomov GN, Ivanova K, Moller IJ, et al. Dental caries-reducing effects of a milk fluoridation project in Bulgaria. J Public Health Dent 1995;55:234–7.
[56] O'Mullane DM. Systemic fluorides. Adv Dent Res 1994;8:181–4.
[57] Shulman JD, Wells LM. Acute fluoride toxicity from ingesting home-use dental products in children, birth to 6 years of age. J Public Health Dent 1997;57:150–8.
[58] Graves RC, Stamm JW. Oral health status in the United States: prevalence of dental caries. J Dent Ed 1985;49:341–51.
[59] Stamm JW. The value of dentifrices and mouthrinses in caries prevention. Int Dent J 1993;43:517–27.
[60] Levy SM. A review of fluoride intake from dentifrice. J Dent Child 1993;61:115–24.
[61] Heilman JR, Kiritsy MC, Levy SM, et al. Fluoride concentrations of infant foods. J Am Dent Assoc 1997;128:857–63.
[62] Singer L, Ophaug R. Total fluoride intake of infants. Pediatrics 1979;63:460–6.
[63] Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine. Dietary reference intakes for calcium phosphorus, magnesium, vitamin D, and fluoride. Washington, DC: National Academy Press; 1997.
[64] Wei SHY, Hattab FN. Fluoride content of dried sea foods [abstract; special issue]. J Dent Res 1987;66:957.
[65] Wiatrowski E, Kramer L, Osis D, et al. Dietary fluoride intake of infants. Pediatrics 1975;55:517–22.
[66] Clovis J, Hargreaves JA. Fluoride intake from beverage consumption. Community Dent Oral Epidemiol 1988;16:11–5.
[67] Shannon IL. Fluoride in carbonated soft drinks. Texas Dent J 1977;95:6–9.
[68] Heilman JR, Levy SM, Kiritsy MC, Wefel JS. Fluoride levels of carbonated soft drinks [abstract]. J Dent Res 1988;77:152.

[69] 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.
[70] Pang DTY, Phillips CL, Bawden JW. Fluoride intake from beverage consumption in a sample of North Carolina children. J Dent Res 1992;71:1382–8.
[71] Shulz EM, Epstein JS, Forrester DJ. Fluoride content of popular carbonated beverages. J Prev Dent 1976;3:27–9.
[72] Chan JT, Koh SH. Fluoride content in caffeinated, decaffeinated and herbal teas. Caries Res 1996;30:88–92.
[73] Smid JR, Kruger BJ. The fluoride content of some teas available in Australia. Aust Dent J 1985;30:25–8.
[74] Kiritsy MC, Levy SM, Warren JJ, et al. Fluoride concentrations of juices and juice drinks. J Am Dent Assoc 1996;127:895–902.
[75] Stannard JG, Shim YS, Kritsineli M, et al. Fluoride levels and fluoride contamination of fruit juices. J Clin Pediatr Dent 1991;16:38–40.
[76] Tinanoff N, Mueller B. Fluoride content in milk and formula for infants. ASDC J Dent Child 1978;45:53–5.
[77] Johnson J, Bawden JW. The fluoride content of infant formulas available in 1985. Pediatr Dent 1987;9:33–7.
[78] Dabeka RW, McKenzie D. Lead, cadmium, and fluoride levels in market milk and infant formulas in Canada. J Assoc Off Anal Chem 1987;70:754–7.
[79] McKnight-Hanes MC, Leverett DH, Adair SM, et al. Fluoride content of infant formulas as a potential factor in dental fluorosis. Pediatr Dent 1988;10:189–94.
[80] Backer-Dirks OB, Jongeling-Eijndhoven JMPA, Flissabaalje TD, et al. Total and free ionic fluoride in human and cow's milk as determined by gas-liquid chromatography and the fluoride electrode. Caries Res 1974;8:181–6.
[81] Warren JJ, Levy SM. Systemic fluoride: sources, amounts and effects of ingestion. Dent Clin N Am 1999;43:695–711.
[82] Dabeka RW, McKenzie AD, Conacher HG, et al. Determination of fluoride in Canadian infant foods and calculation of fluoride intakes by infants. Can J Public Health 1982; 73:188–91.
[83] Featherstone JDB, Shields CP. A study of fluoride intake in New York state residents. Final report: New York State fluoride analysis contract. December 1, 1988.
[84] Guha-Chowdhury N, Brown RH, Shepherd MG. Fluoride intake of infants in New Zealand. J Dent Res 1990;69:1828–33.
[85] Guha-Chowdhury N, Drummond BK, Smillie AC. Total fluoride intake in children aged 3 to 4 years: a longitudinal study. J Dent Res 1996;75:1451–7.
[86] Levy SM, Kohout FJ, Guha-Chowdhury N, et al. Infants' fluoride intake from drinking water alone and added to formula, beverages and food. J Dent Res 1995;74: 1399–407.
[87] Ophaug RH, Singer L, Harland BF. Dietary fluoride intake of 6-month and 2-year-old children in four dietary regions of the United States. Am J Clin Nutr 1985;42:701–7.
[88] Pennington JA. Revision of the Total Diet Study food lists and diets. J Am Diet Assoc 1983;32:166–73.
[89] Rojas-Sanchez F, Kelly SA, Drake KM, et al. Fluoride intake from foods, beverages and dentifrice by young children in communities with negligibly and optimally fluoridated water: a pilot study. Community Dent Oral Epidemiol 1999;27:288–97.
[90] Shulman JD, Lalumandier JA, Grabenstein JD. The average daily dose of fluoride: a model based on fluid consumption. Pediatr Dent 1995;17:13–8.
[91] Grynpas MD. Fluoride effects on bone crystals. J Bone Min Res 1990;5(Suppl 1): S169–75.
[92] Phipps K. Fluoride and bone health. J Public Health Dent 1995;55:53–7.
[93] Phipps K, Orwoll ES, Bevan L. The association between water-borne fluoride and bone mineral density in adults. J Dent Res 1998;77:1739–48.

[94] Warren JJ, Kanellis MJ, Levy SM. Fluorosis of the primary dentition: what does it mean for permanent teeth? J Am Dent Assoc 1999;130:347–56.
[95] Evans RW. Changes in dental fluorosis following an adjustment to the fluoride concentration of Hong Kong's water supplies. Adv Dent Res 1989;3:154–60.
[96] Ishii T, Suckling G. The appearance of tooth enamel in children ingesting water with a high fluoride concentration for a limited period during early tooth development. J Dent Res 1986;65:974–7.
[97] Rozier RG. Reaction paper: appropriate uses of fluoride—considerations for the '90s. J Public Health Dent 1991;51:56–9.
[98] Suga S. Enamel hypomineralization viewed from the pattern of progressive mineralization of human and monkey developing enamel. Adv Dent Res 1989;3:188–98.
[99] Bardsen A. "Risk periods" associated with the development of dental fluorosis in maxillary permanent central incisors: a meta-analysis. Acta Odontol Scand 1999;57:247–56.
[100] Bawden JW. "Where is Waldo?": the timing of fluorosis. J Pub Health Dent 1996;56:5.
[101] Evans RW, Stamm JW. An epidemiological estimate of the critical period during which human maxillary incisors are most susceptible to fluorosis. J Public Health Dent 1991; 51:251–9.
[102] Evans RW, Darvell BW. Refining the estimate of the critical period for susceptibility to enamel fluorosis in human maxillary central incisors. J Public Health Dent 1995;55: 238–249.
[103] Beltrán-Aguilar ED, Griffin SO, Lockwood SA. Prevalence and trends in enamel fluorosis in the United States from the 1930s to the 1980s. J Am Dent Assoc 2002;133:157–65.
[104] Clark DC. Trends in prevalence of dental fluorosis in North America. Community Dent Oral Epidemiol 1994;22:148–52.
[105] Szpunar SM, Burt BA. Trends in the prevalence of dental fluorosis in the United States: a review. J Public Health Dent 1987;47:71–9.
[106] Kumar J, Green E, Wallace W, et al. Trends in dental fluorosis and dental caries prevalence in Newburgh and Kingston, NY. Am J Public Health 1989;79(5):565–70.
[107] Heller KE, Eklund SA, Burt BA. Dental caries and dental fluorosis at varying water fluoride concentrations. J Public Health Dent 1997;57:136–43.
[108] Clark DC, Hann HJ, Williamson MF, et al. Influence of exposure to various fluoride technologies on the prevalence of dental fluorosis. Community Dent Oral Epidemiol 1994; 22:461–4.
[109] Jackson RD, Kelly SA, Katz BP, et al. Dental fluorosis and caries prevalence in children residing in communities with different levels of fluoride in the water. J Public Health Dent 1995;55:79–84.
[110] Williams JE, Zwemer JD. Community water fluoride levels, preschool dietary patterns, and the occurrence of fluoride enamel opacities. J Public Health Dent 1990;50:276–81.
[111] Skotowski MC, Hunt RJ, Levy SM. Risk factors for dental fluorosis in pediatric dental patients. J Public Health Dent 1995;55:154–9.
[112] Warren JJ, Levy SM. A review of fluoride dentifrice related to dental fluorosis. Pediatr Dent 1999;21:265–71.
[113] Lalumandier JA, Rozier RG. The prevalence and risk factors of fluorosis among patients in a pediatric dental practice. Pediatr Dent 1995;17:19–25.
[114] Osuji OO, Leake JL, Chipman ML, et al. Risk factors for dental fluorosis in a fluoridated community. J Dent Res 1988;67:1488–92.
[115] Heifetz SB, Horowitz HS. The amounts of fluoride in current fluoride therapies: safety considerations for children. ASDC J Dent Child 1984;51:257–69.
[116] National Institutes of Health Consensus Development Panel. National Institutes of Health development conference statement—diagnosis and management of dental caries throughout life, March 26–28, 2001. J Am Dent Assoc 2001;132:1153–61.