ARTICLE 1

RISK OF ENAMEL FLUOROSIS IN NONFLUORIDATED AND OPTIMALLY FLUORIDATED POPULATIONS:

CONSIDERATIONS FOR THE DENTAL PROFESSIONAL

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A B S T R A C T

Background. Few studies have evaluated the impact of specific fluoride sources on the prevalence of enamel fluorosis in the population. The author conducted research to determine attributable risk percent estimates for mild-to-moderate enamel fluorosis in two populations of middle-school–aged children.

Methods. The author recruited two groups of children 10 to 14 years of age. One group of 429 had grown up in nonfluoridated communities; the other group of 234 had grown up in optimally fluoridated communities. Trained examiners measured enamel fluorosis using the Fluorosis Risk Index and measured early childhood fluoride exposure using a questionnaire completed by the parent. The author then calculated attributable risk percent estimates, or the proportion of cases of mild-to-moderate enamel fluorosis associated with exposure to specific early fluoride sources, based on logistic regression models.

Results. In the nonfluoridated study sample, sixty-five percent of the enamel fluorosis cases were attributed to fluoride supplementation under the pre-1994 protocol. An additional 34 percent were explained by the children having brushed more than once per day during the first two years of life. In the optimally fluoridated study sample, 68 percent of the enamel fluorosis cases were explained by the children using more than a pea-sized amount of toothpaste during the first year of life, 13 percent by having been inappropriately given a fluoride supplement, and 9 percent by the use of infant formula in the form of a powdered concentrate.

Conclusions. Enamel fluorosis in the nonfluoridated study sample was attributed to fluoride supplementation under the pre-1994 protocol and early toothbrushing behaviors. Enamel fluorosis in the optimally fluoridated study sample was attributed to early toothbrushing behaviors, inappropriate fluoride supplementation and the use of infant formula in the form of a powdered concentrate.

Clinical Implications. By advising parents about the best early use of fluoride agents, health professionals play an important role in reducing the prevalence of clinically noticeable enamel fluorosis.

Enamel fluorosis is a hypomineralization of the enamel caused by the ingestion of an amount of fluoride that is above optimal levels during enamel formation.[1,2] Clinically, the appearance of enamel fluorosis can vary. In its mildest form, it appears as faint white lines or streaks visible only to trained examiners under controlled examination conditions. In its pronounced form, fluorosis manifests as white mottling of the teeth in which noticeable white lines or streaks often have coalesced into larger opaque areas.[2,3] Brown staining or pitting of the enamel also may be present.[2,3] In its most severe form, actual breakdown of the enamel may occur.[2,3]

In recent years, there has been an increase in the prevalence of children seen with enamel fluorosis in both optimally fluoridated and nonfluoridated areas of the United States.[4,5] The greatest relative increase in fluorosis prevalence has occurred in nonfluoridated areas.[4] Dentists and hygienists need to understand the most likely reasons for this increase. This will allow them to advise parents about the most appropriate use of fluoride to prevent caries in their children while minimizing the risk of their children developing enamel fluorosis.

Dating back to the classic research of H. Trendley Dean, it has been well-known that a concentration of approximately 1 part per million fluoride in the drinking water imparts substantial caries protection with the absence of noticeable enamel fluorosis.[6-8]

Since the advent of optimal water fluoridation, other preventive fluoride agents have been introduced. They include ingestible fluoride supplements and fluoride toothpaste, which may be ingested by young children, although it is intended for topical use.[9-11]

Studies suggest that behaviors associated with the early use of fluoride toothpaste—such as the amount of toothpaste usually used when brushing—are associated with enamel fluorosis in both optimally fluoridated and nonfluoridated populations in the United States and elsewhere.[12-25] Studies further suggest that early fluoride supplements use by children living in nonfluoridated areas have been an important risk factor for enamel fluorosis.[21,26-32] Not unexpectedly, the inappropriate use of fluoride supplements by children living in optimally fluoridated areas has been shown to be a strong risk factor for enamel fluorosis.[17,25] The use of infant formula in various forms, before the infant formula industry's voluntary reduction in the fluoride content of its products, also has been associated with enamel fluorosis.[12,17,33] Findings from two recent studies suggest that while the risk of enamel fluorosis associated with infant formula use may no longer exist for children living in nonfluoridated communities, the use of formula in the powdered concentrate form prepared with optimally fluoridated water may continue to be an enamel fluorosis risk factor.[21,25]

While an increasing number of studies have reported estimates of the relative risk or the increased likelihood of enamel fluorosis associated with specific early fluoride exposures, relatively few investigations have evaluated the impact of a specific fluoride-containing agent on the prevalence of enamel fluorosis in the population.[12,15,34] This impact is a function of both the relative risk associated with a specific fluoride-containing agent, as well as the prevalence of exposure to that agent within the population. It is thought to be best measured via estimation of the attributable risk percent,[35] or the percentage of all fluorosis cases that can be explained by exposure to a specific fluoride-containing agent. The attributable risk, therefore, becomes an estimate of the potential reduction in cases that would occur were the associated exposure modified or eliminated. Because children may be exposed to several different fluoride-containing agents during the tooth-development period, the most accurate attributable risk percent estimate for a specific fluoride-containing agent should be adjusted for exposure to any other fluoride-containing agents.[4,35] To date, only two investigations have reported adjusted attributable risk percent estimates[15,34]; and only one of these investigations has reported these estimates along with adjusted confidence intervals, which gives the reader the best sense of the statistical significance of those estimates.[34] That study also was the only one to have reported findings from the investigation of a U.S. population.[34]

A study of Canadian children who were current residents of an optimally fluoridated area reported that 72 percent of the fluorosis cases could be attributed to beginning to brush teeth with fluoride toothpaste during the first two years of life.[12] In this same study, 22 percent of the cases were attributed to the use of infant formula.

A study of Australian children who also resided in an optimally fluoridated area reported that 47 percent of the fluorosis cases could be explained by a history of swallowing toothpaste at a young age, while 55 percent of the fluorosis cases seen in this study could be explained by the early cessation of breast-feeding, with the implication that these infants were switched to the use of infant formula.[15]

A study of children in Connecticut who grew up in optimally fluoridated communities reported that 71 percent of the cases could be attributed to "usually" brushing more than once a day and "usually" using more than a pea-sized amount of toothpaste during the first eight years.[34] Twenty-five percent of these cases were attributable to children having been inappropriately given a fluoride supplement during the first eight years of their lives.[34]

Understanding attributable risk information reported in the literature is important; dentists and hygienists need to be able to provide the parents of young children with appropriate advice regarding the early use of fluoride toothpaste and fluoride supplements. In this article, I report on results of research I performed to determine attributable risk percent estimates for mild-to-moderate enamel fluorosis in two populations of middle-school–aged children born after the 1978 fluoride supplement dosage revision[36,37] and after the decision by U.S. infant formula manufacturers to reduce and control the fluoride content of their products[38,39] (effective for those born in 1980 and after). Because comprehensive, surface-specific analyses of the relative risk percent estimates associated with enamel fluorosis in these two populations have been previously reported,[21,25] key findings from those reports will be only briefly reviewed in this article.

MATERIALS AND METHODS

Detailed descriptions of the methods used in my previous investigations are published elsewhere[21,25]; therefore, only a brief summary follows. All study procedures involving human subjects were approved by the University of Connecticut Health Center Institutional Review Board. The study subjects consisted of middle-school–aged children who had grown up in either six nonfluoridated Massachusetts and Connecticut communities or five optimally fluoridated Connecticut communities.

Among the subjects who grew up in nonfluoridated areas of Massachusetts and Connecticut, it was found that children who were reported to have begun brushing with fluoridated toothpaste during the first two years of life and who reported they usually brushed more than once per day had an approximately three- to fourfold increase in the risk of enamel fluorosis, depending on the specific enamel surfaces affected.[21] In this same population, children who were reported to have used a fluoride supplement throughout the second through eighth years of life had an approximately two- to eightfold increase in the risk of enamel fluorosis, again depending on the specific enamel surfaces affected.[21]

The subjects in the second population grew up in optimally fluoridated areas in Connecticut.[25] These areas had begun fluoridation many years before these children were born, and when the water departments were contacted, they indicated that episodes of below-optimum fluoridation were rare and brief over the lifetimes of the subjects. In this population, it was found that children who were reported to have usually brushed with more than a pea-size amount of toothpaste and who were reported to have usually brushed more than once per day had a six- to eightfold increase in the risk of enamel fluorosis, depending on the specific surfaces affected.[25] Children in these optimally fluoridated areas who inappropriately were given fluoride supplements had an approximately six- to 10-fold increase in the risk of enamel fluorosis, again depending on the specific enamel surfaces affected.[25] In this population, the reported use of infant formula in the form of a powdered concentrate produced an approximately four- to 10-fold increase in the risk of enamel fluorosis, once again depending on the specific surfaces affected.[25]

Two trained examiners measured enamel fluorosis using the Fluorosis Risk Index.[40] For the attributable risk analyses presented in this article, I included a subject as a fluorosis case if he or she had mild-to-moderate enamel fluorosis as defined by Møller[41] that was characterized by the presence of paper-white streaking, coalescence of opacities or both on more than 50 percent of two or more enamel surface zones, anywhere throughout the dentition.[41] A fluorosis control was defined as any subject who was fluorosis-free throughout the dentition.

Two examiners conducted random, blind inter- and intraexaminer reliability examinations daily throughout the data collection period. There were few cases (approximately 2 percent) of subjects showing signs of more severe fluorosis, which was characterized by the presence of brown staining or pitting. Therefore, I included these few subjects in the analyses with the rest of the cases.

I retrospectively obtained fluoride exposure history via a self-administered, closed-ended questionnaire that was mailed to the parents of all case and control subjects. Parents were offered $20 for return of the completed questionnaire. This questionnaire had been pretested and used in two fluorosis risk investigations.[17,27] The subject's name was handwritten on the cover of the questionnaire and into each of the questions within the questionnaire. This was done to help keep parents with several children mindful of the specific child we were asking about.

For each quarter of the first year of life—birth through 3 months, 4 through 6 months, and so on—parents were asked to indicate, by checking the appropriate box, whether the subject's main source of food was breast milk, ready-to-feed infant formula, formula in the form of liquid concentrate, formula in the form of powdered concentrate, cow's milk or solid food. They also were asked to do this for the second year of the children's lives as a whole. Then they were asked to write in the usual brand of infant formula used, which allowed me to determine whether the formula was milk- or soy-based. For each of the first eight years, parents were asked to write in the city and state (country if not the United States) where the subject lived for each year. Also for each of the first eight years, parents were asked to indicate by checking the appropriate box whether the subject was given plain vitamins without fluoride, a vitamin drop with fluoride, a vitamin tablet with fluoride, a fluoride drop alone, a fluoride tablet alone or nothing. Parents were asked to indicate by circling the best choice whether the subject usually did not brush, usually brushed once a day or usually brushed more than once a day during the first eight years, and by circling the best drawing to indicate whether the subject usually placed a pea-sized amount or more of toothpaste on his or her toothbrush when brushing during the first eight years. Parents were asked to indicate by circling the appropriate age at which the subjects began to brush and at what ages they helped the subjects brush their teeth. For each of the first eight years, parents were asked to write in the subjects' places of residence. Parents also were asked to indicate whether they used bottled water or a tap water filter for more than two of the first eight years. Finally, they were asked to indicate their relationship to the subjects and to indicate by circling the appropriate ages during which of the subjects' first eight years they had lived with them.

I included for analysis only subjects whose questionnaires were completed by parents who had resided with the subjects for the entire eight-year survey period. I assessed questionnaire reliability by having a randomly drawn sample of respondents complete a second questionnaire that was mailed at least one month after the completion of the first.

I included in the nonfluoridated group analysis only data from subjects born after 1979 who were residents of a nonfluoridated community for the entire eight-year survey period. For the optimally fluoridated group analysis, I included only data from subjects born after 1979 who were residents of an optimally fluoridated community for the entire eight-year survey period. I determined the fluoridation status of prior residences other than in the survey communities using the Fluoridation Census.[42]

I derived adjusted attributable risk percent estimates and adjusted 95 percent confidence intervals, or CIs, individually for early fluoride exposures found to be associated with an increased risk of mild-to-moderate enamel fluorosis, based on logistic regression analyses.[43,44] I derived these attributable risk percent estimates separately for the nonfluoridated study sample and for the optimally fluoridated study sample. I included variables found to have been either important predictors of enamel fluorosis or important covariates in the relative risk analyses[21,25] in each of the attributable risk analyses.

RESULTS

A total of 1,091 subjects (94 percent of those enrolled and 15 percent of those eligible to enroll) were examined for fluorosis in the nonfluoridated study sample. A total of 867 subjects (95 percent of those enrolled and 14 percent of those eligible to enroll) were examined for fluorosis in the optimally fluoridated study sample. Intra- and interexaminer agreement on case vs. control status was 98.9 percent and 93.8 percent, respectively (κ = 0.93 and 0.73, respectively), in the nonfluoridated sample and 100 percent and 86 percent, respectively (κ = 1.0 and 0.70, respectively), in the optimally fluoridated sample. The prevalence of mild-to-moderate enamel fluorosis was 39 percent in the nonfluoridated sample and 34 percent in the optimally fluoridated sample. Eighty-four percent of the cases from the nonfluoridated communities and 74 percent of cases from the optimally fluoridated communities involved the maxillary anterior teeth.

The questionnaire return

TABLE 1

ESTIMATED PERCENTAGE OF ENAMEL FLUOROSIS CASES ATTRIBUTABLE TO SPECIFIC FLUORIDE SOURCES IN A NONFLUORIDATED POPULATION.

FLUORIDATION SOURCE	ATTRIBUTABLE RISK PERCENT ESTIMATES*	ATTRIBUTABLE RISK 95 PERCENT CI†
Supplementation History‡		
Supplemented Year 1	29	–6-52
Supplemented Years 2 Through 8	65	34-81
Toothbrushing History§		
Began During Years 1 and 2; Brushed More Than Once per Day	34	18-47
Began During Years 1 and 2; Brushed Once per Day	8	–2-17
Began After Year 2; Brushed More Than Once per Day	6	–4-14
Used More Than a Pea-sized Amount of Toothpaste	45	–7-72

* Estimate of cases attributable to each specific fluoride source based on logistic regression modeling.[21] Note that individual attributable risk percents do not add up to 100 percent, as fluoride supplementation and toothbrushing history are not mutually exclusive exposures.[43]
† CI: Confidence interval.
‡ Reference group: no supplementation during each of the identified periods.
§ Reference group: began after year 2; brushed once per day.

rate was 90 percent in the nonfluoridated sample and 91 percent in the optimally fluoridated sample. A 12 percent reliability sample in the nonfluoridated sample and a 16 percent reliability sample in fluoridated revealed an average agreement between the second and first questionnaire responses of 87 percent for both study samples.

A total of 250 subjects with mild-to-moderate enamel fluorosis and 179 fluorosis-free controls were available in the nonfluoridated study sample for analysis, after exclusions based on year of birth, fluoridation history or completion of the questionnaire by someone other than parents who had lived with their children throughout the entire eight-year survey period. These subjects ranged in age from 10 to 13 years of age (mean = 12.5 years), and 57 percent were girls. Eighty-six percent of these subjects were lifelong residents of their current communities.

A total of 180 subjects with mild-to-moderate fluorosis and 54 fluorosis-free control subjects were available in the fluoridated study sample for analysis, again after exclusions based on year of birth, fluoridation history or completion of the questionnaire by someone other than parents who had lived with their children throughout the entire eight-year survey period. These subjects ranged in age from 10 to 14 years of age (mean = 12.9 years), and 56 percent were girls.

Tables 1 and 2 show the multiple logistic-regression–derived, adjusted attributable risk percent estimates for these two study samples. Individual attributable risk percents do not add to 100 percent, since the variables studied in both samples were not mutually exclusive exposures.[43]

For the nonfluoridated study sample, Table 1 shows that an estimated 65 percent of the cases could be attributed to or explained by exposure to fluoride supplements during the second through eighth year of life. Thirty-four percent of the cases in this sample could be explained by a history of having begun to brush with toothpaste during the first two years and having usually brushed more than once per day. The logistic-regression–derived test for

TABLE 2

ESTIMATED PERCENTAGE OF ENAMEL FLUOROSIS CASES ATTRIBUTABLE TO SPECIFIC FLUORIDE SOURCES IN AN OPTIMALLY FLUORIDATED POPULATION.

FLUORIDATION SOURCE	ATTRIBUTABLE RISK PERCENT ESTIMATE*	ATTRIBUTABLE RISK 95 PERCENT CI†
Supplementation History‡		
Supplemented Years 1 Through 2	13	6-20
Toothbrushing History§		
More Than a Pea-sized Amount of Toothpaste, More Than Once per Day	46	25-61
More Than a Pea-sized Amount of Toothpaste, Once per Day	22	8-35
Pea-sized Amount of Toothpaste, More Than Once per Day	2	–6-10
Formula as Powdered Concentrate**	9	3-15

* Estimate of cases attributable to each specific fluoride source based on logistic regression modeling.[24] Note that individual attributable risk percents do not add up to 100 percent, as fluoride supplementation, toothbrushing history and infant formula use are not mutually exclusive exposures.[43]
† CI: Confidence interval.
‡ Reference group: no fluoride supplementation years 1 through 2.
§ Reference group: pea-sized amount of toothpaste, once per day.
** At 10 to 12 months of age. Referent group: no infant formula used.

trend across the three toothbrushing exposure categories was statistically significant, suggesting a dose response effect; however, the negative CI limits for two of the toothbrushing exposure categories indicate that the analysis cannot say with 95 percent certainty that cases could be attributed to these two exposure histories. While not statistically significant, the findings suggested that perhaps 45 percent of the observed cases could be attributed to the usual early use of greater than a pea-sized amount of toothpaste when brushing.

For the study subjects who grew up in optimally fluoridated communities, Table 2 shows that an estimated 13 percent of the cases could be explained by the inappropriate use of fluoride supplements during the first two years of life. Forty-six percent of the cases could be explained by a history of having usually used more than a pea-sized amount of toothpaste when brushing and usually having brushed more than once per day. The test for trend across the three toothbrushing exposure categories was statistically significant, again supporting the presence of a dose-response effect. A clear association with age when brushing began was not observed in this study sample, when adjusted for usual toothbrushing frequency and amount of toothpaste used.

Table 2 also shows that 9 percent of the cases could be explained by a history of having used infant formula in the form of a powdered concentrate as the main source of food, especially during the last quarter of the first year. There was no suggestion of an association with ready-to-feed infant formula and no significant association was observed with liquid concentrate formula. The reported use of either bottled water or a tap water filter was not statistically significantly associated with fluorosis in the analyses from either nonfluoridated or optimally fluoridated populations.

DISCUSSION

Attributable risk percent estimates associated with enamel fluorosis are useful in assessing the public health impact of particular fluoride exposures.

Children in the United States today are exposed to a variety of fluoride sources during early childhood. Some sources, such as fluoride supplements, are intended to be ingested. Others, such as fluoride toothpaste, are intended for topical use but are nevertheless ingested by preschool-aged children who typically have not begun to expectorate any or enough of the toothpaste with which they brush.[45,46] It is important when estimating the attributable risk percent specific to a particular fluoride exposure that this estimate be adjusted for the effects of the other exposures. In this way, the estimate of the effect of a particular exposure is not biased by the other exposures. It also is important to recognize that the effect of exposure to a specific fluoride source within a population is always in the context of exposure to that source along with exposure to the other fluoride sources within that population. In this way, the fluorosis impact of one fluoride source among several can be estimated, and appropriate professional and public health action can be taken.

In this study, approximately two-thirds of mild-to-moderate enamel fluorosis cases observed in optimally fluoridated areas and at least one-third of mild-to-moderate enamel fluorosis cases observed in nonfluoridated areas could be attributed to or explained by habits related to the early use of fluoride toothpaste. Three potentially important behaviors associated with early toothbrushing are when toothbrushing began, the usual daily frequency of toothbrushing and the usual amount of toothpaste used during brushing. All three of these behaviors are indicators of the overall fluoride ingestion associated with early toothbrushing.

In the nonfluoridated study population, the age at which toothbrushing began and the usual frequency of toothbrushing were most significantly associated with enamel fluorosis. While not statistically significant, these findings suggest that as much as 45 percent of the enamel fluorosis cases could be explained by a history of having usually used more than a pea-sized amount of toothpaste when brushing.

In the optimally fluoridated study population, the usual amount of toothpaste used when brushing and the usual daily frequency of toothbrushing were most significantly associated with enamel fluorosis. The statistically significant trends observed with early toothpaste use in both study samples suggests a dose-response relationship.

A previous investigation of a Connecticut study population who grew up in optimally fluoridated communities estimated that approximately 70 percent of enamel fluorosis cases could be attributed to early toothbrushing behaviors.[34] Findings from Canadian and Australian studies of children who were current residents of optimally fluoridated areas suggested that many of the enamel fluorosis cases seen in those investigations also could be attributed to early toothbrushing habits.[12,15] This study's findings from the optimally fluoridated study sample are consistent with those past reports. Importantly, this study's findings from the nonfluoridated study sample suggest that early toothpaste use behaviors may affect the prevalence of enamel fluorosis, regardless of whether the community is optimally fluoridated.

These findings reinforce the important opportunity and need for dentists and hygienists to guide the parents of preschool-aged children in proper fluoride toothpaste use. Specifically, dental professionals should advise parents to supervise their preschool-aged children during toothbrushing and be sure that the children use only a small pea-sized amount of toothpastes when brushing. This advice should be given and followed regardless of whether the children live in an optimally fluoridated or nonfluoridated area. Parents should encourage their children to expectorate the toothpaste at the earliest possible age rather than swallow it, avoid toothpastes with flavors that would encourage young children to wish to eat the toothpaste, and keep toothpaste and all other fluoride-containing products out of the reach of preschool-aged children. These findings further support the call for a lower-fluoride-concentration toothpaste, specifically for use by preschool-aged children.[34,47-49]

The findings of this study indicate that nearly two-thirds of the cases of mild-to-moderate enamel fluorosis observed in nonfluoridated areas could be attributed to or explained by the early use of fluoride supplement. Subjects in this investigation would have been given fluoride supplements under the pre-1994 protocol; these findings strongly support the new, lower dosage fluoride supplementation protocol, which has been accepted by both the

TABLE 3

REVISED FLUORIDE SUPPLEMENTATION SCHEDULE.*

AGE	FLUORIDE CONCENTRATION IN THE DRINKING WATER		
	Less Than 0.3 ppm†	0.3 to 0.6 ppm	More Than 0.6 ppm
Birth to 6 Months	None	None	None
6 Months to 3 Years	0.25 milligrams per day‡	None	None
3 to 6 Years	0.50 mg/day	0.25 mg/day	None
6 to 16 Years	1.00 mg/day	0.50 mg/day	None

* Revised schedule accepted by the American Dental Association,[50] the American Academy of Pediatric Dentistry and the American Academy of Pediatrics.
† ppm: Parts per million.
‡ 2.2 mg sodium fluoride contain 1 mg fluoride ion.

American Dental Association and the American Academy of Pediatrics (Table 3).[50,51]

The ADA Guide to Dental Therapeutics[50] is a good resource on the use of fluoride supplements, as well as other fluoride-containing compounds. Dentists and hygienists should evaluate the fluoride content of a child's drinking water, while keeping in mind that the child may have access to more than one drinking water source during the day, both at home and in a child-care setting, for example. If the child's drinking water is not from a municipal water supply of known fluoride concentration, the drinking water sources must be tested for their fluoride content. Then, a proper decision regarding what fluoride supplementation, if any, is appropriate can be made based on the protocol in Table 3. By doing this, dentists can avoid inappropriately prescribing fluoride supplements to children who already are drinking adequately fluoridated water. It also is important to determine whether children are receiving a fluoride supplement as part of a multiple vitamin prescribed by a physician. Dentists should ask parents to bring to the office any vitamin preparations their children are taking so the vitamins can be evaluated directly. Dentists also should ask parents to inform them if the children's drinking water sources change.

The use of bottled drinking water complicates the process, as bottled water's fluoride content can vary markedly, and manufacturers are not required to list the fluoride content.[52] A one-time test of the fluoride content of bottled water may not be sufficient to prescribe a fluoride supplement, as a child's family might change the brand of bottled water it drinks or the fluoride concentration could change.

My current findings indicate that 13 percent of the cases of mild-to-moderate enamel fluorosis observed in optimally fluoridated areas could be attributed to or explained by the inappropriate use of fluoride supplements during the first two years of children's lives while they lived in these optimally fluoridated areas. This is not surprising. The use of fluoride supplements by children living in optimally fluoridated areas has never been recommended by any professional organization, given the likelihood of causing an above-optimal ingestion of fluoride.[50, 51,53-55] Fortunately, the percentage of cases attributable to inappropriate fluoride supplementation was relatively low in this study population and was approximately one-half that reported in the only previously published report of the attributable risk associated with enamel fluorosis and inappropriate fluoride supplementation.[34] Nevertheless, this finding illustrates the need for dentists and hygienists to serve as a source of guidance to parents as to the proper use of fluoride supplements.

The findings of this investigation suggest that nearly 10 percent of the enamel fluorosis cases in optimally fluoridated areas could be explained by having used infant formula in the form of a powdered concentrate during the first year. I observed no suggestion of an association between enamel fluorosis and infant formula—in any form—in the nonfluoridated population. These findings support the continued concern that the use of powdered concentrate formula mixed with optimally fluoridated water still may have an impact on the prevalence of enamel fluorosis in optimally fluoridated areas.[55,56]

To my knowledge, this is the first investigation reporting attributable risk percent estimates associated with infant formula use after the U.S. formula manufacturers' voluntary decision in 1979 to reduce the fluoride in their products. Therefore, other studies will need to be conducted to confirm these findings. In the interim, however, it may be prudent to recommend to parents living in optimally fluoridated areas who are feeding formula to their infants, that they either use a ready-to-feed formula or prepare formula from concentrate using bottled water with a known low-fluoride concentration. Care should be taken, however, to explain to the parent that drinking optimally fluoridated water by itself is not a risk factor for noticeable enamel fluorosis,[6,7] and that drinking optimally fluoridated water has proven important caries preventive benefits.[7]

The questionnaire used in these investigations originally was judged to possess content validity (that is, adequacy of the questions to measure what the questionnaire is suppose to measure)[57,58] by me, my colleagues, nondental–trained pretesters and a National Institutes of Health scientific review panel. Throughout its use in five separate investigations of several thousand subjects, there have been few questions raised by respondents relative to the meaning of questions. Beyond this, questions in this questionnaire have shown considerable predictive validity[57,58] as used in the specific investigation reported in this article, as well as in previous investigations in which it has been used. For example, as hypothesized in previous toothpaste ingestion studies,[47] adjusted multivariate analyses have consistently shown specific early toothpaste-use variables to be associated with enamel fluorosis diagnosed by examiners blind to the children's fluoride exposure histories. This supports the likelihood that the questionnaire has measured what it intended to measure.

In this type of study (case-controlled), guessing on the part of questionnaire respondents always diminishes the observed association between fluoride exposure and fluorosis or hides it entirely.[59] In contrast, if responses were biased such that a history of exposure to one fluoride source really reflected a true exposure to a different fluoride source, then the potential for an observed spurious association would exist. In this situation, however, adjustment for the true risk factor by use of a multivariate analyses would reveal a true lack of association between the spurious factor and fluorosis. Therefore, the use of fully adjusted, multivariate analyses in this investigation lends further support to the validity of observed associations.

CONCLUSIONS

The findings reported in this article suggest that early toothbrushing habits have an important impact on the prevalence of mild-to-moderate enamel fluorosis in both nonfluoridated and optimally fluoridated areas. At least one-third of the fluorosis cases in nonfluoridated areas and two-thirds of the cases in optimally fluoridated areas could be explained by specific patterns of early fluoride toothpaste use.

Approximately two-thirds of mild-to-moderate enamel fluorosis cases in nonfluoridated areas could be explained by the use of fluoride supplements under the pre-1994 supplementation protocol. Inappropriate use of fluoride supplements explained 13 percent of fluorosis cases in optimally fluoridated areas. An additional 9 percent of fluorosis cases in optimally fluoridated areas were explained by the use of infant formula in the form of a powdered concentrate. This relationship with infant formula use was not seen in nonfluoridated areas.

These findings reinforce the important role that health professionals can have in reducing the prevalence of enamel fluorosis in U.S. children today and suggest that much of the clinically noticeable enamel fluorosis seen today could be prevented by specific changes in early childhood behaviors. In particular, providing the parent of a young child with appropriate advice regarding the early use of fluoride toothpaste and fluoride supplements may have a significant impact on the prevalence of enamel fluorosis in both nonfluoridated and optimally fluoridated populations. ■

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