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ABSTRACT

Background. Fluoride dentifrice is a primary means of preventing childhood caries, but it is also an important risk factor for fluorosis. The authors examine the influence of fluoride dentifrice ingestion on fluorosis of the permanent incisors.

Methods. Participants in the Iowa Fluoride Study received questionnaires at regular intervals concerning fluoride sources. The authors assessed fluorosis using the fluorosis risk index. They estimated daily fluoride ingestion from dentifrice, diet and fluoride supplements and divided the amount by kilograms of body weight. The statistical analysis related fluoride ingestion to fluorosis in the permanent incisors.

Results. In bivariate analyses, mild fluorosis was significantly related to ingestion of fluoride dentifrice at ages 24 and 36 months ($P = .02$ for both). After the authors adjusted for fluoride ingested from dietary sources, logistic regression showed a significant association between fluorosis and dentifrice ingestion at age 24 months ($P = .04$).

Conclusions. The study results suggest that fluorosis of the permanent incisors is influenced by ingestion of fluoride dentifrice during the first three years of life. Further research is needed to assess total intake of fluoride as a risk factor for fluorosis.

Clinical Implications. These results support recommendations that young children use only a pea-sized amount of dentifrice. Parents should supervise young children as they brush their teeth with fluoride dentifrice.

Key Words. Dentifrice; fluorosis; children; fluoride; incisors.
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Widespread use of fluoride in many forms, including dentifrice, has been largely responsible for the decline in dental caries in most developed nations.[1] However, many of these nations have had increases in the prevalence of dental fluorosis.[2,3]

BACKGROUND

Fluoride's effects on caries prevention have been well-documented, as has its role in dental fluorosis.[4-12] Fluoride dentifrice is an important component of fluoride use and ingestion by infants and preschoolers; therefore, it is a risk factor for fluorosis. Because of the risk of fluorosis, the American Dental Association has recommended that young children use only a small, pea-sized amount of fluoride toothpaste at each brushing.[13] The Centers for Disease Control and Prevention also recommends this and stresses supervision of fluoride dentifrice use in children younger than 6 years.[1] The American Academy of Pediatric Dentistry's Clinical Guideline on Fluoride Therapy is consistent with regard to these recommendations and recommends using a pea-sized amount of fluoride dentifrice.[14]

Approximately 98 percent of all dentifrice sold in the United States contains fluoride. Several studies

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have assessed different aspects of fluoride dentifrice use, and they found that it is used widely among all age groups.[5,6,15-22] It is important to better understand the impact of ingestion of fluoride dentifrice among very young children as it relates to fluorosis risk. Several studies found an association between dental fluorosis and fluoride dentifrice use; the results generally demonstrated increased fluorosis prevalence with early and/or increased use of fluoride dentifrice.[4-12] However, these studies generally have been retrospective, and the "optimal" balance of fluoride use and intake for prevention of dental caries and fluorosis is not yet fully understood.

Enamel fluorosis is a condition that results from exposure to excessive fluoride during enamel formation. Studies generally suggest that the early maturation stage of enamel development is more critical with regard to the development of fluorosis than is the earlier, secretory stage.[23-25] Most studies[23,25-30] indicate that early-erupting permanent teeth (incisors and first molars) appear to be most susceptible to fluorosis during the first two to three years of life, although two other studies[31,32] suggest different, perhaps later, critical periods for fluorosis development.

Therefore, the purpose of this article is to describe the influence of estimated fluoride dentifrice ingestion at ages 16, 24 and 36 months (both individually and combined) on fluorosis experience in the early-erupting permanent dentition.

SUBJECTS AND METHODS

We obtained the data for this project from the Iowa Fluoride Study (IFS),[5,16,33-35] a longitudinal investigation of fluoride intake among a cohort recruited at birth from eight Iowa hospitals from March 1992 through February 1995.[6] The University of Iowa Institutional Review Board approved the project, and we obtained informed consent from the mothers before the investigation. Parents provided consent and their children provided assent before dental examinations at ages 7 through 11 years.

The IFS has collected large amounts of data during the past 12 years, with the aim of relating estimated total fluoride intake to exposures to dental fluorosis and dental caries. While the mothers and newborns were in the hospital postpartum, mothers provided information about their age, education, family income and number of children in the household. Trained study staff informed them about the protocol to be followed thereafter.[6,16]

IFS staff sent questionnaires to the mothers when their children were aged 6 weeks and 3 months and then at three-, four- or six-month intervals thereafter. Questionnaires included detailed questions concerning the previous time period with regard to water sources; ingestion of water by itself, other beverages, and water mixed with other beverages and foods; patterns of use of dietary fluoride supplements; toothbrushing patterns; and use of fluoride dentifrice. For this article, we used information concerning fluoride exposures and toothbrushing at ages 16, 24 and 36 months.

Oral examinations. One of two trained dentist examiners (J.W. or Michael Kanellis, D.D.S., M.S.) conducted one mixed-dentition caries and fluorosis examination in each subject sometime between the ages of 7 and 11 years (mean age, 9.1 years). They used the fluorosis risk index (FRI) to assess fluorosis in permanent teeth.[36] The FRI assesses fluorosis on four enamel zones (incisal edge/occlusal table, incisal third, middle third and gingival third) on each tooth, with the zones grouped according to the age at which enamel formation is initiated.

For the examinations, the teeth were dried with cotton gauze and trained staff recorded the scores for each zone of the permanent first molars and incisors. The examiners used Russell's criteria to differentiate fluorosis from demarcated nonfluoride opacities.[37] We excluded the gingival third zone from these analyses because it was not consistently fully erupted.

Fluorosis and nonfluorosis cases. We included in the analyses all subjects for whom questionnaires were returned at ages 16, 24 and 36 months and those who received a mixed-dentition examination (N = 343). We defined fluorosis cases as those in which two or more of the eight permanent incisors had definitive fluorosis (according to FRI criteria in which a score of 2 is assigned if 50 percent or more of a zone has definitive fluorosis versus a score of 3 for severe fluorosis, which also involves staining, pitting and/or other deformity). We defined nonfluorosis cases as those in which there was no definitive fluorosis in the permanent incisors. Twenty-three subjects who had one incisor with fluorosis were excluded from these analyses.

The dental examiners conducted duplicate examinations in 39 subjects to assess interexaminer reliability (using percentage agreement and

kappa statistics). They calculated fluoride intake from dentifrice using parental estimates of brushing frequency per day, amount of dentifrice used at each brushing, the proportion of dentifrice that was swallowed at each brushing and fluoride concentration of the dentifrice (obtained by linking the subject's brand of dentifrice to our study documentation).[5,6,16]

The IFS assessed water sources from home, child care and bottled water using assays of wells and filtered waters, links to public documentation of municipal water sources and assays of most major recorded brands of commercial bottled water.

Fluoride intake. We estimated fluoride intake from water by multiplying each subject's water intake by his or her water source fluoride concentrations and product-specific water fluoride assay results.[22,38] We conducted fluoride assays of water and most beverages using a fluoride ion-specific electrode (Model 9609, Orion Research, Boston) and an ion analyzer (Model 920, Orion Research) after using a total ionic strength adjustment buffer (TISAB) (TISAB II buffer 94909, Orion Research) to provide constant ionic strength, free up the fluoride and adjust the pH.[38] Quality control efforts included random samples read again at the end of the day to verify electrode accuracy, repeat readings on standards to confirm the standard curve and analysis of approximately 6 to 20 percent of samples in duplicate.[38] Mean reproducibility was 97 to 99 percent.[38,39] Solids and selected beverages were analyzed with a modified Taves hexamethyldisiloxane microdiffusion method,[38,40] and the fluoride concentration of the resulting solution then was assessed using the method as described above. More than 20 percent of samples were done in duplicate with mean reproducibility of 98 percent.[38]

Parents estimated the quantities of beverages and foods prepared with water that their children consumed during the previous week, and they documented the type of beverage and amount of added water. Specifically, parents reported daily ingested quantities of water by itself, milk, ready-to-drink juices and juice drinks, carbonated beverages, beverages mixed from frozen concentrate, beverages mixed from powdered concentrate, foods made with almost all water (for example, gelatin, dry soup), foods made with some water (for example, canned soup) and foods cooked in and absorbing substantial amounts of water (for example, rice, pasta, oatmeal). We determined the fluoride intake from beverages other than water and the selected foods by multiplying the daily intake in each category by the average fluoride levels for those specific categories from our extensive series of assays.[39,41]

We calculated fluoride intake from prescribed fluoride supplements using parental estimates of frequency and dosage, paired with study data documenting the amount of fluoride contained in the supplement.[42,43] Estimates of the amount of fluoride dentifrice used were based on parents' questionnaire responses to a series of diagrams of toothbrushes holding varying amounts of dentifrice. The parent selected the diagram that best depicted the amount that the child used most often to clean his or her teeth and estimated the amount that the child swallowed.

We combined fluoride intakes from beverages and selected foods with fluoride intake from dietary supplements to estimate fluoride ingestion from sources other than dentifrice. Both the fluoride intake from dentifrice and the intake from diet/supplements were estimated in milligrams of fluoride per kilogram body weight. We calculated cumulative estimates (16 to 36 months) of fluoride ingestion from dentifrice and diet/supplements using the area-under-the-curve (AUC) trapezoidal method (expressed as milligrams of fluoride per kilogram of body weight [mg F/kg bw] per day).

Statistical analysis. We obtained descriptive statistics for baseline measures and for toothbrushing behaviors at ages 16, 24 and 36 months. We calculated medians, along with 25th and 75th percentiles, to summarize fluoride ingestion from dentifrice for the study sample. Because fluoride ingestion measures did not uniformly exhibit normal distribution qualities (that is, the data were skewed), tests of association used the Wilcoxon rank sum test (fluorosis cases versus nonfluorosis cases) and the Kruskal-Wallis test for multilevel baseline measures. Multiple logistic regression models at each time point and for 16 to 36 months (AUC) tested associations between fluorosis and fluoride ingested from dentifrice and fluoride ingested from diet and supplements. We added a joint test of combined intake to each model.

We assessed the reliability of questionnaire data for a portion of participants in the IFS via follow-up telephone calls within two weeks of when we received the questionnaires. Telephone

interviewers assessed recall agreement with regard to use of fluoride supplements, toothbrushing frequency and type of water used at home (that is, tap, bottled or both). They did not ask parents to recall types or amounts of dietary fluoride intake because of the complexity and variability of early childhood diets. We used a software program (SAS system version 8, SAS Institute, Cary, N.C.) to conduct the statistical analysis and considered *P* levels below .05 to be significant.

RESULTS

Subjects for whom questionnaires were returned at ages 16, 24 and 36 months are characterized in Table 1. The sample (N = 343) was composed of approximately one-half boys and one-half girls, with large proportions being the first child in the family and having white mothers. Mothers and fathers generally were well-educated, with almost one-half having at least a four-year college degree. Only 11 percent of the families had a yearly income below $20,000 at baseline.

Sixty-six percent of all children showed no signs of permanent incisor fluorosis (nonfluorosis cases) and 27 percent had fluorosis on two or more incisors (cases). Nearly all fluorosis seen in this study was mild, with only three subjects exhibiting severe fluorosis with staining, pitting or both. (Another 7 percent of children had definitive fluorosis on only one incisor and were excluded from analyses.) Reliability assessment at different ages showed high agreement with regard to the use of fluoride supplements ($\kappa = 0.97$), toothbrushing frequency (weighted $\kappa = 0.79$) and type of water used at home ($\kappa = 0.83$). Our assessment of interexaminer reliability with regard to diagnoses of fluorosis showed 76 percent agreement ($\kappa = 0.53$).

Table 2 (page 650) summarizes dentifrice use patterns and toothbrushing behaviors. Among those who brushed regularly, frequency increased gradually with age, with 82 percent brushing at least once per day by age 36 months. However, only 65 percent of these subjects (at age 16 months), 90 percent (at age 24 months) and 96 percent (at age 36 months) were using fluoridated dentifrice.

Eleven percent of children who used fluoridated dentifrice used amounts estimated to contain 0.50 mg fluoride or more per brushing at age 16 months, and the percentage increased to 29 percent at age 24 months and 45 percent at age 36 months. Parents reported that children at ages 16 and 24 months ingested most of the fluoridated dentifrice used; however, by age 36 months, children swallowed less dentifrice.

Using Kruskal-Wallis tests, we assessed differences in AUC (that is, ages 16 to 36 months) fluoride ingestion from dentifrice by sex, first child status, mother's educational level, father's educational level and family income (all variables assessed at recruitment when the child was born). The children in midrange-income families ($30,000 to $49,999) exhibited higher levels of dentifrice ingestion than did those from low- and high-income families ($P = .04$; data not shown). No other differences were significant. When comparing fluorosis cases with nonfluorosis cases (Table 3, page 650), we observed significant differences in fluoride ingestion from dentifrice at ages 24 months, 36 months and AUC ages 16 to 36 months.

To assess the importance of fluoride ingested from dentifrice relative to other sources of ingested fluoride in predicting fluorosis, we considered four separate logistic regression models (ages 16 months, 24 months, 36 months and 16 to 36 months). Because none of the demographic characteristics examined were significantly associated with fluorosis, each model included only a variable for fluoride ingested from dentifrice, as well as a second variable for fluoride ingested from diet and fluoride supplements combined.

Table 4 (page 650) shows a significant association between permanent incisor fluorosis and dietary fluoride ingestion (from beverages, selected foods and fluoride supplements) at age 16 months ($P = .02$), age 36 months ($P = .0001$) and AUC ages 16 to 36 months ($P = .003$). Fluorosis also was significantly associated with fluoride ingestion from dentifrice at age 24 months ($P = .04$), while results did not reach significance ($P = .07$) for AUC 16- to 36-month fluoride ingestion from dentifrice. All models except the 16-month model showed that fluorosis and combined fluoride intake (from beverages, selected foods, fluoride supplements and dentifrice) were highly associated (all $P < .01$).

DISCUSSION

In this study, we found generally consistent, positive relationships between ingestion of fluoride dentifrice and fluorosis experience, even though the associations were not statistically significant at all time periods. This evidence of an associa-

TABLE 1

Description of the study sample.

EXPLANATORY VARIABLE	PERCENTAGE OF ALL SUBJECTS (N = 343*)	PERCENTAGE OF NON-FLUOROSIS CASES (n = 227)	PERCENTAGE OF FLUOROSIS CASES (n = 93)	χ^2 P VALUE
Sex				
Male	49	48	48	1.00
Female	51	52	52	
First Child?				
Yes	42	42	45	.59
No	58	58	55	
Mother's Race				
White	98.5	98	99	.66
Other	1.5	2	1	
Annual Family Income†				
< $20,000	11	10	10	
$20,000-$29,999	14	14	13	
$30,000-$39,999	22	24	22	.87
$40,000-$49,999	20	22	19	
$50,000-$59,999	13	12	17	
≥ $60,000	19	18	19	
Mother's Education†				
High school/GED‡ or less	15	16	11	.46
Some college	21	21	24	
Two-year college degree	15	16	14	
Four-year college degree	29	27	34	
Graduate/professional school	20	20	17	
Father's Education†				
High school/GED or less	25	27	21	
Some college	17	14	20	
Two-year college degree	11	10	12	.45
Four-year college degree	28	27	30	
Graduate/professional school	20	22	16	
Number of Permanent Incisors With Fluorosis				
None	66	100	0	
One	7	0	0	
Two	12	0	45	—§
Three	6	0	23	
Four	4	0	16	
Five to six	2	0	7	
Seven to eight	2	0	9	

* Twenty-three of the 343 subjects who had fluorosis on one incisor only were excluded from the analyses.
† At the child's birth.
‡ GED: General equivalency diploma.
§ Not applicable.

tion between fluoride dentifrice ingestion and dental fluorosis is consistent with the results of previous studies relating dentifrice use to fluorosis.[7-12] For example, in a study conducted by Pendrys and colleagues,[9] mild or moderate fluorosis of early erupting permanent teeth was associated strongly with frequent toothbrushing before age 8 years.

Our study demonstrated not only that fluorosis is associated with higher total fluoride intake at ages 24 and 36 months, but also that fluorosis is associated with fluoride intake from dentifrice alone at age 24 months. This is an age at which children generally have established toothbrushing habits, but they still swallow substantial amounts of dentifrice. The amount of fluoride ingested from dentifrice can be high relative to their small body size.

First two years of life. Previous studies have shown an increased risk of developing dental fluorosis to be associated with greater use of fluoride dentifrice during the first two years of life. Osuji and colleagues[44] reported that children who began brushing with fluoridated dentifrice between ages 6 and 24 months were at an 11 times greater risk of developing dental fluorosis than children who did not begin brushing before age 24 months. Other studies have reported that the early matu-

TABLE 2

Dentifrice use and toothbrushing behavior, by age.*

EXPLANATORY VARIABLE	PERCENTAGE OF SUBJECTS BY AGE (N = 343)		
	16 MONTHS	24 MONTHS	36 MONTHS
Among All Subjects			
Brush teeth	90	100	100
Among Subjects Who Brush Teeth			
Use fluoridated dentifrice	65	90	96
Use nonfluoridated dentifrice	3	2	1
Do not use dentifrice	32	8	3
Toothbrushing Frequency (per Day)			
Less than once	35	25	18
Once	48	51	57
Twice	14	23	24
More than twice	4	2	1
Among Dentifrice Users			
Use dentifrice flavored for children	45	50	60
Among Fluoridated Dentifrice Users			
Estimated amount of fluoride per brushing 0.50 mg† or more	11	29	45
Estimated percentage of dentifrice swallowed			
≤25	13	7	21
50	5	9	13
≥75	82	85	66

* Source: Franzman and colleagues.[6]
† mg: Milligrams.

ration stage (about 24 months of age) for maxillary central incisors is the most sensitive to fluoride exposure.[25,45] Pendrys[8] concluded that 34 percent of fluorosis cases in a study population living in a nonfluoridated community could be attributed to children having begun brushing with fluoridated dentifrice during the first two years of life and usually having brushed more than once per day.

Table 3 shows the differences in fluoride dentifrice ingestion between the children who had fluorosis and those who did not. At age 16 months, children with and without fluorosis had similar intakes of fluoride dentifrice, and intake tended to be low. At age 24 months, however, fluoride intake from dentifrice was much higher overall, and the median intake of children who had fluorosis was somewhat greater than that for those who did not have fluorosis (0.017 mg F/kg bw versus 0.010 mg F/kg bw). This suggests that higher levels of fluoride from ingested dentifrice at age 24 months can lead to permanent tooth fluorosis. Although most of the children in this study did not ingest large amounts of fluoridated dentifrice at age 16 months, dentifrice still should be considered a potential risk factor for children who start brushing regularly at this age and ingest large amounts of fluoridated dentifrice.

TABLE 3

Daily fluoride ingestion* from dentifrice.

AGE AT DENTIFRICE INGESTION (MONTHS)	DEFINITIVE FLUOROSIS ON PERMANENT INCISORS						P VALUE†
	No			Yes (Two or More Incisors)			
	No. of subjects‡	Median daily fluoride ingestion*	(25th, 75th percentiles*)	No. of subjects§	Median daily fluoride ingestion*	(25th, 75th percentiles*)	
16	220	0.002	(0.000, 0.008)	89	0.002	(0.000, 0.010)	.61
24	220	0.010	(0.003, 0.020)	89	0.017	(0.006, 0.035)	.02
36	220	0.012	(0.005, 0.026)	89	0.016	(0.007, 0.031)	.02
16-36 AUC¶	220	0.011	(0.005, 0.020)	89	0.013	(0.009, 0.028)	.02

* In milligrams of fluoride per kilogram of body weight.
† Based on Wilcoxon rank sum test.
‡ Weight data were missing for seven of 227 subjects.
§ Weight data were missing for four of 93 subjects.
¶ AUC: Area under the curve.

TABLE 4

Logistic regression analysis of permanent incisor fluorosis cases.

MODEL	FLUORIDE* SOURCE	*DF*†	ADJUSTED ODDS RATIO‡	95 PERCENT CONFIDENCE INTERVAL	*P* VALUE FOR COMPONENT	*P* VALUE FOR COMBINED INTAKE
16 Months	Diet and supplements Dentifrice	1 1	1.39 0.97	1.08-1.78 0.74-1.26	.02 .81	.15
24 Months	Diet and supplements Dentifrice	1 1	1.24 1.30	0.97-1.59 1.02-1.65	.10 .04	.007
36 Months	Diet and supplements Dentifrice	1 1	1.66 1.23	1.28-2.15 0.95-1.57	.0001 .12	.0001
16-36 Months (AUC§)	Diet and supplements Dentifrice	1 1	1.49 1.26	1.15-1.92 0.99-1.61	.003 .07	.0004

* In milligrams of fluoride per kilogram body weight.
† *DF*: Degrees of freedom.
‡ Odds ratio and confidence interval were adjusted by the standard deviation. Odds ratio reflects increased odds of fluorosis associated with a change in fluoride intake of 1 standard deviation.
§ AUC: Area under the curve.

Den Besten[25] reviewed the mechanism and timing of fluoride's effects on developing enamel and reported that, although the maturation stage is most sensitive to the effects of fluoride, the duration of exposure to fluoride before the early maturation stage does affect the severity of enamel fluorosis. Considering that the first two to three years of life generally are believed to be most critical to fluorosis development on early erupting permanent teeth,[26-30] our study results suggest that children should use dentifrice carefully and use only a pea-sized amount, particularly at about 24 months of age. Parents or guardians should supervise children closely when brushing to monitor the amount of dentifrice used, the frequency of brushing and the effectiveness of brushing. This recommendation is consistent with recommendations from the American Dental Association,[13] the American Academy of Pediatric Dentistry[14] and the Centers for Disease Control and Prevention[1] regarding use of fluoride dentifrice.

Study strengths and limitations. The IFS data allow for a unique evaluation of toothbrushing behaviors of children. Its longitudinal design, the substantial number of respondents and the specific nature of its questionnaires provide detailed estimates of systemic fluoride intake. However, the cohort was not composed of a diverse representation of families in the United States; thus, generalizations should be made with caution. In addition, we must keep in mind that parents reported the data and investigators did not directly observe the toothbrushing behaviors of children. Finally, some information was missing as a result of some parents' failure to return some questionnaires, which may have affected the results. These analyses were limited to the subset of subjects for whom questionnaires were returned at all three time points. Also, with little dental fluorosis observed beyond the mild stage, it was not possible to assess associations with more involved dental fluorosis.

CONCLUSION

The results of this study affirm the link between use of fluoride dentifrice and the development of mild dental fluorosis; in particular, they suggest that this relationship is most pronounced at about age 24 months. The findings suggest that health professionals, including dentists, pediatricians, family physicians and others, need to emphasize the proper use of small quantities of dentifrice among toddlers, with appropriate parental supervision, to limit the amount of ingested dentifrice. Reducing fluoride ingestion from dentifrice at this age likely will limit the development and severity of fluorosis on the esthetically important permanent incisors. ■

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