Patterns of Fluoride Intake from Birth to 36 Months

Steven M. Levy, DDS, MPH; John J. Warren, DDS, MS; Charles S. Davis, PhD; H. Lester Kirchner, PhD; Michael J. Kanellis, DDS, MS; James S. Wefel, PhD

Abstract

Objectives: *Dental fluorosis prevalence has increased in the United States, Canada, and other nations due to the widespread availability of fluoride in many forms, with fluoride ingestion during the first three years of life appearing most critical in fluorosis etiology. With few contemporary studies of fluoride ingestion in this age group, the purpose of this paper is to describe patterns of estimated fluoride ingestion from birth to 36 months of age from water, dentifrice, and dietary fluoride supplements and combined.* ***Methods:*** *Repeated responses to separate series of questions about water intake, use of fluoride dentifrice, and use of fluoride supplements were collected by questionnaire as part of the longitudinal Iowa Fluoride Study and used to estimate fluoride intake. Estimated intake is reported by source and combined at different ages. Effects of subject age and other covariates on fluoride intake were assessed using regression methods appropriate for the analysis of correlated data.* ***Results:*** *For most children, water fluoride intake was the predominant source, especially through age 12 months. Combined daily fluoride intake increased through 9 months, was lower at 12 and 16 months, and increased again thereafter. Mean intake per unit body weight (bw) was about 0.075 mg F/kg bw through 3 months of age, 0.06 mg F/kg bw at 6 and 9 months, 0.035 mg F/kg bw at 12 and 16 months, and 0.043 mg F/kg bw from 20–36 months. Depending on the threshold chosen (e.g., 0.05 or 0.07 mg F/kg bw), variable percentages of the children exceeded the levels, with percentages greatest during the first 9 months. Regression analyses showed fluoride intake (mg F/kg bw) from 1.5–9 months to decrease with increasing child's age, mother's age, and mother's education, with a complex three-way interaction among these factors. From 12–20 months, fluoride intake increased with increasing child age and decreased with increasing mother's age. No statistically significant relationships were found for fluoride intake from 24–36 months.* ***Conclusions:*** *There is considerable variation in fluoride intake across ages and among individuals. Longitudinal studies may be necessary to fully understand the relationships between fluoride ingestion over time and development of fluorosis. [J Public Health Dent 2001;61(2):70-77]*

Key Words: fluoride, fluoride ingestion, dentifrice, fluoride supplements.

The levels of fluoride exposures early in life are important not only in relation to caries prevention, but also in the development of dental fluorosis. In particular, fluoride ingestion during the first three years of life appears to be most critical in fluorosis etiology (1-3). Unfortunately, there have been relatively few contemporary studies of fluoride ingestion in this age group, so that our understanding of fluorosis development is limited.

Previous studies of fluoride ingestion have been mostly cross-sectional and focused on single sources of intake such as foods and beverages, dentifrice, or dietary fluoride supplements. The earliest studies of fluoride intake were diet surveys showing that although absolute fluoride intake tended to increase with age, when expressed on a per body weight basis, intake peaked during the first few months of life (4-6). These early diet studies suggested a so-called "optimal" range of fluoride intake of 0.05–0.07 mg F per kilogram body weight, which has become the main reference range when discussing fluoride intake. Subsequent studies using several different methods found that dietary fluoride intake generally was higher in fluoridated areas (7–11), but that dietary fluoride intake varied considerably. Some studies reported mean fluoride intakes at or above "optimal" intakes, but other means fell far below this range (5-11).

Studies of fluoride ingestion from dentifrice have found that younger children generally ingest a higher proportion of dentifrice than do older children, often ingesting over half of the dentifrice used per brushing (10-15). Several studies have found that dentifrice use and ingestion varies considerably among children, with some children ingesting more than 1 gram of dentifrice (1 mg fluoride) per brushing (10,16).

Dietary fluoride supplements are an important source of fluoride ingestion for those children receiving them and it has been estimated that in the United States about 15–16 percent of children aged 4 years or younger use supplements (17). Although compliance with dietary fluoride supplement regimens is often poor and the actual amount ingested on a daily basis is far less than the prescribed dosage (18), some children can have fluoride ingestion from dietary supplements alone that exceeds the so-called "optimal" range.

Although studies of fluoride ingestion from individual sources provide some useful data, it is obviously much more important to the understanding of fluorosis etiology to characterize total fluoride intake. Unfortunately, because of the complexity of assessing fluoride intake due to the multiplicity

Send correspondence and reprint requests to Dr. Levy, N330 DSB, University of Iowa, Iowa City, Iowa 52242. E-mail: steven-levy@uiowa.edu. Dr. Warren is affiliated with the Department of Preventive and Community Dentistry, Dr. Davis is with the Department of Biostatistics, Dr. Kanellis is with the Department of Pediatric Dentistry, and Dr. Wefel is with the Department of Pediatric Dentistry and the Dows Institute for Dental Research, all at the University of Iowa. Dr. Kirchner is with the Department of Pediatrics, Case Western Reserve University, Cleveland, OH. Manuscript received: 4/25/00; returned to authors for revision: 6/27/00; accepted for publication: 8/10/00.

of fluoride sources, only a few studies have attempted to estimate total fluoride intake by simultaneously assessing intakes from major sources, including foods, beverages, dentifrice, and supplements.

In New Zealand, Guha-Chowdhury et al. (10) estimated fluoride intake from diet, dentifrice, and supplements among 12-month-old children. They found fluoride intake to be lower in nonfluoridated areas, and that in both nonfluoridated and fluoridated areas fluoride intake was fairly low, with mean values of 0.020 mg/kg and 0.033 mg/kg, respectively. However, some individuals in fluoridated areas had intakes above 0.10 mg/kg body weight. In a similar study of 3–4-year-olds (10), Guha-Chowdhury et al. again found lower fluoride intake among those in nonfluoridated areas, with mean intakes of 0.027 mg/kg and 0.036 mg/kg in nonfluoridated and fluoridated communities, respectively. A study of fluoride intake from foods, beverages, and dentifrice by young children from Indiana and Puerto Rico (11) estimated much higher intakes than in New Zealand, with means in each community exceeding 0.05 mg/kg body weight. In both Indiana communities, roughly half the children exceeded the upper limit of "optimal" fluoride intake, 0.07 mg/kg body weight.

Although these latter studies characterize fluoride exposures in early childhood more comprehensively than did previous studies, they are nonetheless limited by their cross-sectional design. Since fluorosis may be related to a cumulative, longitudinal effect of ingested fluoride, such designs are not as desirable for understanding fluorosis etiology. The purpose of the present study is to describe patterns of estimated fluoride ingestion from birth to 36 months of age from water, dentifrice, and dietary fluoride supplements, and combined, as well as demographic factors associated with the patterns of intake.

Methods

Data for this study were collected as part of the Iowa Fluoride Study, a longitudinal investigation of fluoride intake among a birth cohort recruited from eight Iowa hospitals from March 1992 through February 1995 (18–20). While the mothers and newborns were in the hospital postpartum and after informed consent was obtained, mothers provided information at baseline about their age, education, family income, and number of children in the household and were informed about the protocol to be followed thereafter. Questionnaires then were sent to the mothers when the children were aged 6 weeks, and at ages 3, 6, 9, 12, 16, 20, 24, 28, 32, and 36 months. Nonrespondents were sent follow-up mailings after three weeks and, when necessary, again after six weeks. Thus, the response times varied from a few days to several weeks or more after the initial mailing.

Questionnaires included detailed questions concerning the previous time period assessing water sources and ingestion of water by itself and mixed with other beverages and foods (21), patterns of use of dietary fluoride supplements (18), and toothbrushing patterns and use of fluoride dentifrice (19). Using these series of questions, separate estimates were calculated for daily fluoride intake from water, supplements (18), and dentifrice (19) in mg. Specifically, a modified food frequency questionnaire was used to assess daily number of servings and ounces of water by itself; water for beverages prepared from frozen or powder concentrates; water mixed with concentrated soups, Jello, etc.; and water from preparing rice and pasta (21). For individual (well) water sources or when filtration was in use, fluoride levels were determined by individual fluoride assay with fluoride-ion specific electrode (22). This was done initially, whenever sources or filtration changed, and annually. For those on public water systems without filtration, assay results available from the Iowa State Health Department were used.

The quantity of water ingested was multiplied by the home water fluoride level to get an estimate of fluoride intake from water. For dietary fluoride supplements, questions assessing use overall, number of weeks of use, number of days per week, product, and fluoride dosage were used to estimate average daily fluoride intake from supplements (18). Similarly, questions about frequency of brushing, dentifrice brands, quantity of dentifrice used (selecting from a series of pictures of toothbrushes with different quantities of dentifrice), and proportion of dentifrice ingested, as determined by parental report, were used to estimate the dentifrice (19). Then a combined estimate of fluoride intake from these three sources was made in mg F/day. Parental reports of the children's body weights were used to calculate estimated daily fluoride intake in mg per kg body weight (mg F/kg bw) for each response.

It was not feasible to validate parental responses, but some reliability assessments were conducted for approximately 225 questionnaires 7–10 days after the initial questionnaires were completed. Percentage agreement for questions concerning water filtration status were about 96–97 percent (kappa 0.87–0.99), concerning water consumption was 94 percent (kappa=0.75), concerning use of dietary fluoride supplements was 99.6 percent (kappa=0.97), concerning toothbrushing frequency was 81 percent (kappa=0.77), and concerning use of dentifrice was 93.1 percent (kappa=0.74).

Two types of analyses of the fluoride data were conducted. To first provide descriptive tabulations and plots of the results, the assessment times were treated as discrete categories. The second type of analysis focused on the development of models assessing the effects of subject age and other covariates on fluoride intake. In these analyses, the actual assessment times (ages in days) were used.

In the descriptive summaries of the fluoride intake data, each response was categorized discretely as occurring at the closest of 1.5, 3, 6, 9, 12, 16, 20, 24, 28, 32, or 36 months. In this way, every observation is considered to have occurred at one and only one of the scheduled measurement times. This categorization occasionally resulted in a subject having multiple responses at a given assessment time. To obtain a single measurement per time point, the observation closest to the scheduled measurement time was used, except if the observation closest to the scheduled measurement time had more incomplete data (missing values) than the other observation(s) from that time period, then the observation with the fewest missing components was used. Using the categorized data set, summary statistics (mean, standard deviation, selected percentiles) were computed at each time point. This was completed using all available data at each assessment time.

In developing models related to the total fluoride intake, all assessments from each subject were used (not just one unique assessment per scheduled measurement time). Since there are multiple, correlated measurements per subject, the Generalized Estimating Equations (GEE) regression methodology for correlated data (23) was used to model the effects of subject age and other covariates on total fluoride intake. Since total fluoride intake is essentially continuous, the identity link function was used. Since subject age was a time-dependent covariate, the independence working correlation model was used (24). This was also an appropriate choice given both the unequal number and unbalanced spacing of observations. The estimated regression parameters and their robust standard errors were computed using the repeated measures capabilities of the SAS GENMOD procedure (25).

Due to age-related patterns of fluoride intake, three prespecified age ranges were separately modeled: 0–10.5 months, 10.5–22 months, and 22–38 months. For each of these three models, the following covariates were considered: subject age; subject sex (1=male, 0=female); mother's race (1=white, 0=nonwhite); mother's age (1=30+ years, 0=younger than 30 years); mother's educational level (two indicator variables); first child (1=yes, 0=no); number of children living in the household (two indicator variables); and baseline household income level (<$30,000 per year vs $30,000+ per year). Since approximately one-third of the mothers had a four-year college degree, and more than half of the remainder had a high-school degree, two indicator variables for mother's educational level were used: HSGRAD=1 if mother had a high school degree, but not a four-year college degree, and 0 otherwise; and COLLGRAD=1 if mother had a four-year college degree, and 0 otherwise. For number of children, NKIDS2=1 if there were two children living at home, and 0 otherwise; and NKIDS3=1 if there were three or more children living at home, and 0 otherwise. Additional covariates related to the father's age and education were considered. However, due to the substantial numbers of missing values for these variables, these were not used. In the model-building process, observations were excluded when the values of one or more covariates included in the particular model were missing.

For each of the three age ranges, the steps used in the modeling process were as follows:

1. An initial model including all covariates was fit. Age was treated as a discrete variable and the age effect was parametrized using orthogonal polynomial coefficients. Based on the results of Wald tests of the nonlinear components of the age effect, the lowest-order polynomial that provided an adequate fit to the data was determined.

2. A model including all covariates was fit, but now age was treated as a continuous variable using the appropriate number of polynomial terms based on the results of step 1. The joint significance of multiple degree of freedom (df) effects were tested using Wald tests.

3. The least significant terms were sequentially eliminated from the previous model and the tests of the joint significance of multiple df effects repeated. This process was repeated to develop a parsimonious final model.

4. Steps 2 and 3 were repeated independently, this time treating age as a discrete variable, but still using the lowest-order polynomial that provided an adequate fit to the data. Any differences in process or outcome between the two methods were noted.

5. Based on the final model identified in step 3, the existence of interactions between age and each of the covariates included in the final model was investigated. If there was evidence of interaction, the final model was revised to include appropriate interaction terms.

Although this procedure did not guarantee that the "best" model was found, it provided an objective approach to addressing the questions of interest.

TABLE 1
Characteristics of the Sample (at Baseline)

Variable	Category	Percent
Sex	Male	49.7
	Female	50.3
Mother's age	<20 years	7.5
	20–24 years	20.6
	25–29 years	31.0
	30–34 years	27.1
	≥35 years	13.8
Father's age	<20 years	1.2
	20–24 years	12.0
	25–29 years	29.9
	30–34 years	32.1
	≥35 years	24.9
Mother's education	Up to high school	30.5
	Some college	32.3
	College graduate or more	37.2
Father's education	Up to high school	34.6
	Some college	27.8
	College graduate or more	37.7
Family income	<$20,000	23.8
	$20,000–$39,999	35.7
	≥$40,000	40.5
Race	White	95.1
	Other	4.9
First child	Yes	44.3
	No	55.7
Plans to breastfeed	Yes	64.5
	No	35.5

FIGURE 1
Percentage Ingesting Fluoride from Water, Supplements, and Dentifrice by Age (Assuming Discrete Time Points)

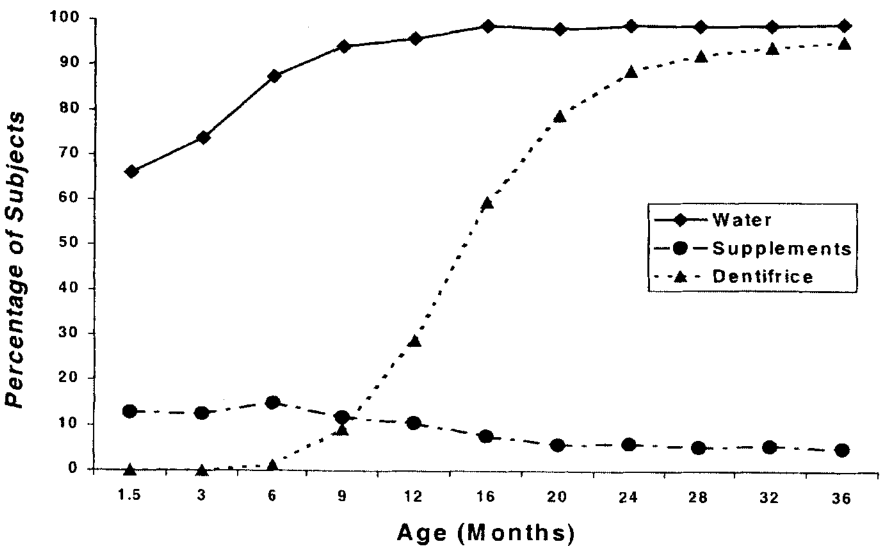
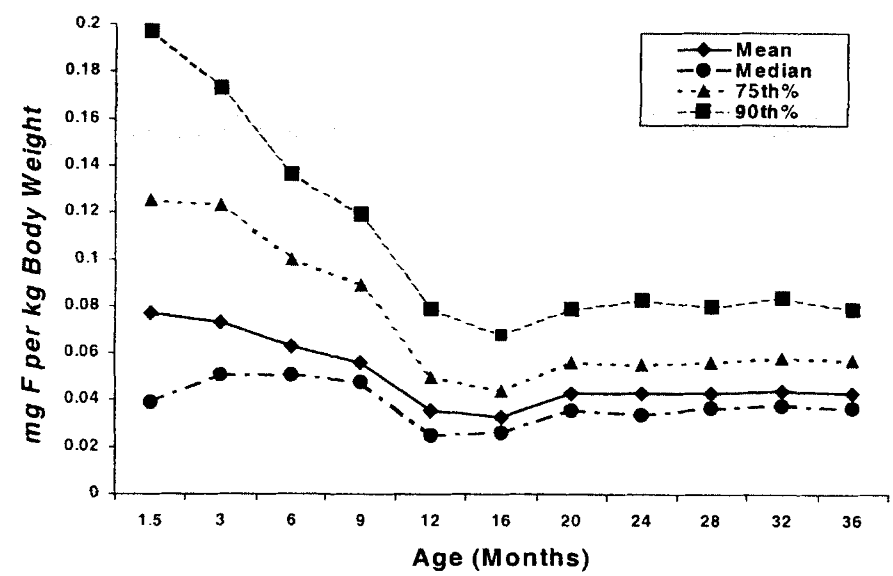


FIGURE 2
Estimated Mean and Median Fluoride Intake from Dentifrice, Supplements, and Water per Unit Body Weight (mg F/kg bw)



Results

Table 1 shows the demographic characteristics for the 1,387 subjects at baseline. Subjects were of relatively high socioeconomic status, with most mothers (79%) aged 20 to 34 years and most fathers (87%) aged 25 years or older. About two-thirds of both mothers and fathers had some college education, and more than three-quarters had family incomes of $20,000 or greater.

Home water fluoride levels varied for some individuals with changes in water sources and filtration, but were generally consistent. At the varying ages, about 18–22 percent were <0.3 ppm F, 7–12 percent were 0.30–0.60 ppm, 33–41 percent were 0.61–1.00 ppm, 27–32 percent were 1.01–1.50 ppm, 2–3 percent were 1.51–2.00 ppm, and 1 percent were above 2.00 ppm.

Figure 1 shows the percentages of subjects grouped at each discrete age who reportedly ingested some fluoride from each of water, supplements, and dentifrice. The majority received some water fluoride at all ages, increasing to ≥95 percent by 9 months. About 11–15 percent used dietary fluoride supplements through 12 months, declining thereafter to 5 percent at 36 months. Fluoride dentifrice ingestion occurred for 1 percent and 9 percent at 6 months and 9 months, respectively, increasing to 29 percent and 60 percent at 12 and 16 months, and to 93 percent by 28 months. Seventy-three percent received fluoride from at least one of the three sources at 6 weeks, with ≥96 percent from 9 months on.

Table 2 summarizes the discrete frequency distributions of estimated fluoride intake from water, supplements, dentifrice, and combined in mg per day. Estimated mean daily fluoride intake from dentifrice was less than or equal to 0.10 mg through 16 months and 0.19 to 0.29 mg from 20–36 months. However, the 90th percentiles were 0.50 or greater for ≥20 months and the maximum values exceeded 1.0 mg for ≥6 months. Because small percentages used dietary fluoride supplements, mean intake was consistently low; however, the maximum intakes were generally close to 1.0 mg. Daily mean water fluoride intake was about 0.35–0.48 mg through 9 months, and about 0.26–0.34 mg thereafter. Ninetieth percentiles were approximately 1.0 mg through 9 months and 0.56–0.74 mg thereafter. Maximum values were 6–8 mg through 12 months, due to consumption of a liter or more of high fluoride (5–6 ppm) well water. Combined fluoride intake averaged 0.37–0.45 mg through 3 months, about 0.50 mg at 6 and 9 months, 0.36 mg at 12 and 16 months, and 0.50–0.63 mg thereafter. Ninetieth percentiles approached or exceeded 1.0 mg, while maximum values were 6–8 mg through 12 months (from the water, as above) and 1.9–3.8 mg thereafter. The distributions were skewed, with means consistently greater than the medians and substantial variation shown by the large standard deviations relative to the means. For fluoride from water, from dentifrice, and the three sources combined, the 90th percentiles were substantially larger than the means and medians.

The discrete frequency distribution of estimated fluoride intake from water, supplements, dentifrice, and

TABLE 2
Distributions of Estimated Fluoride Intake from Water, Supplements, Dentifrice, and Combined, by Age (mg)

	Age (mos.)	N	Weight (kg) Mean (SD)	Fluoride (mg) Mean (SD)	Min	Percentiles of Fluoride Intake 10th	25th	50th	75th	90th	Max
Dentifrice	1.5	1,070	4.90 (0.87)	0.000 (0.000)	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	3.0	1,202	6.26 (1.02)	0.000 (0.000)	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	6.0	1,032	7.96 (1.09)	0.002 (0.041)	0.000	0.000	0.000	0.000	0.000	0.000	1.313
	9.0	916	9.16 (1.23)	0.013 (0.081)	0.000	0.000	0.000	0.000	0.000	0.000	1.313
	12.0	777	10.10 (1.26)	0.038 (0.136)	0.000	0.000	0.000	0.000	0.010	0.109	1.750
	16.0	700	11.03 (1.42)	0.102 (0.207)	0.000	0.000	0.000	0.018	0.109	0.250	1.531
	20.0	637	11.93 (1.52)	0.191 (0.270)	0.000	0.000	0.010	0.109	0.250	0.500	1.750
	24.0	627	12.69 (1.61)	0.257 (0.312)	0.000	0.000	0.041	0.125	0.375	0.656	1.750
	28.0	588	13.51 (1.77)	0.267 (0.305)	0.000	0.010	0.063	0.125	0.375	0.750	2.250
	32.0	597	14.23 (1.95)	0.290 (0.315)	0.000	0.021	0.063	0.219	0.438	0.750	2.625
	36.0	523	14.95 (2.01)	0.278 (0.292)	0.000	0.018	0.063	0.188	0.438	0.750	1.688
Supplements	1.5	1,059	4.90 (0.88)	0.014 (0.045)	0.000	0.000	0.000	0.000	0.000	0.042	0.375
	3.0	1,193	6.26 (1.02)	0.018 (0.060)	0.000	0.000	0.000	0.000	0.000	0.042	0.833
	6.0	1,023	7.96 (1.09)	0.019 (0.063)	0.000	0.000	0.000	0.000	0.000	0.053	1.000
	9.0	922	9.17 (1.22)	0.014 (0.052)	0.000	0.000	0.000	0.000	0.000	0.024	0.500
	12.0	794	10.10 (1.27)	0.015 (0.054)	0.000	0.000	0.000	0.000	0.000	0.013	0.500
	16.0	729	11.03 (1.41)	0.011 (0.054)	0.000	0.000	0.000	0.000	0.000	0.000	1.000
	20.0	655	11.91 (1.50)	0.008 (0.038)	0.000	0.000	0.000	0.000	0.000	0.000	0.250
	24.0	646	12.68 (1.61)	0.008 (0.052)	0.000	0.000	0.000	0.000	0.000	0.000	1.000
	28.0	616	13.49 (1.80)	0.012 (0.068)	0.000	0.000	0.000	0.000	0.000	0.000	1.000
	32.0	612	14.21 (1.95)	0.013 (0.079)	0.000	0.000	0.000	0.000	0.000	0.000	1.000
	36.0	536	14.94 (2.02)	0.013 (0.079)	0.000	0.000	0.000	0.000	0.000	0.000	1.000
Water	1.5	1,048	4.90 (0.87)	0.351 (0.492)	0.000	0.000	0.000	0.133	0.586	0.947	6.408
	3.0	1,178	6.27 (1.02)	0.429 (0.525)	0.000	0.000	0.000	0.264	0.740	1.065	6.656
	6.0	1,019	7.95 (1.09)	0.469 (0.481)	0.000	0.000	0.064	0.374	0.784	1.041	7.562
	9.0	918	9.16 (1.22)	0.476 (0.471)	0.000	0.023	0.101	0.391	0.777	1.021	7.904
	12.0	779	10.09 (1.27)	0.307 (0.372)	0.000	0.019	0.065	0.207	0.434	0.740	5.989
	16.0	714	11.03 (1.42)	0.255 (0.229)	0.000	0.025	0.084	0.202	0.358	0.556	1.769
	20.0	643	11.93 (1.49)	0.305 (0.254)	0.000	0.036	0.102	0.249	0.450	0.618	1.657
	24.0	630	12.67 (1.60)	0.289 (0.264)	0.000	0.035	0.102	0.222	0.394	0.594	2.109
	28.0	582	13.49 (1.79)	0.298 (0.273)	0.000	0.035	0.101	0.232	0.421	0.616	2.198
	32.0	609	14.21 (1.95)	0.314 (0.296)	0.000	0.032	0.099	0.253	0.442	0.642	2.912
	36.0	532	14.96 (2.02)	0.341 (0.299)	0.000	0.047	0.127	0.266	0.461	0.712	1.724
Combined	1.5	1,038	4.90 (0.87)	0.365 (0.490)	0.000	0.000	0.000	0.190	0.592	0.959	6.408
	3.0	1,169	6.27 (1.02)	0.448 (0.520)	0.000	0.000	0.033	0.304	0.746	1.065	6.656
	6.0	1,000	7.96 (1.09)	0.493 (0.483)	0.000	0.004	0.098	0.399	0.803	1.074	7.562
	9.0	899	9.16 (1.23)	0.505 (0.478)	0.000	0.032	0.139	0.414	0.791	1.041	7.904
	12.0	755	10.10 (1.27)	0.360 (0.396)	0.000	0.033	0.107	0.259	0.503	0.790	5.989
	16.0	674	11.04 (1.42)	0.367 (0.311)	0.000	0.059	0.142	0.293	0.495	0.775	1.894
	20.0	615	11.94 (1.50)	0.504 (0.356)	0.005	0.135	0.249	0.434	0.667	0.950	2.157
	24.0	603	12.66 (1.58)	0.547 (0.414)	0.004	0.139	0.264	0.441	0.722	1.132	2.880
	28.0	552	13.51 (1.78)	0.580 (0.429)	0.016	0.165	0.293	0.495	0.770	1.085	3.763
	32.0	582	14.22 (1.95)	0.622 (0.428)	0.000	0.198	0.311	0.529	0.820	1.180	3.287
	36.0	506	14.95 (2.02)	0.634 (0.425)	0.009	0.195	0.327	0.539	0.826	1.163	2.976

combined intake per body weight expressed in mg F/kg bw per day also was positively skewed and with substantial variation in results. Means and standard deviations of body weights (kg) are shown in Table 2 to allow interested readers to conduct their own general calculations of ranges of fluoride intake per kg bw, because a full table is not shown. Estimated daily mean intake from dentifrice was 0.001, 0.004, and 0.009 mg F/kg bw at 9, 12, and 16 months, respectively, and then 0.016–0.021 mg F/kg bw from 20–36 months. Ninetieth percentiles for

20–36 months were 0.042–0.054 mg F/kg bw, and maximums exceeded 0.120 mg F/kg bw from 6 months on. Mean daily supplement fluoride intake was consistently low (0.001–0.003 mg F/kg bw), although maximums were 0.13–0.15 mg F/kg bw through 6 months. Mean estimated daily water fluoride intake declined from 0.070–0.074 mg F/kg bw at 1.5–3 months to 0.060 and 0.053 at 6–9 months, to 0.02–0.03 mg F/kg bw from 12–36 months. Ninetieth percentiles were 0.115–0.197 up to 9 months, 0.075 at 12 months, and 0.045–0.053 thereafter. Maximum levels exceeded 0.90 mg F/kg bw through 9 months, were about 0.64 mg F/kg bw at 12 months, and were 0.11–0.20 mg F/kg bw at all ages thereafter.

Estimated daily combined fluoride intake closely paralleled water fluoride intake through 12 months, and thereafter was substantially greater than water fluoride intake. Estimated combined means declined from 0.073–0.077 mg F/kg bw at 1.5–3 months to 0.036–0.043 mg F/kg bw from 12–36 months. Ninetieth percentiles were 0.119–0.197 mg F/kg bw to 9 months and 0.068–0.084 thereafter, with maximums about 0.200–1.794 mg F/kg bw. Figure 2 shows the patterns by age for the means, medians, and 75th and 90th percentiles of estimated fluoride intake per kg body weight from the three sources combined. Mean and median fluoride intake per kg body weight was greatest through 6 months, lowest at 12 and 16 months, and then slightly higher and quite steady thereafter. Seventy-fifth and 90th percentiles were greatest initially, declined through 16 months, and were then slightly higher and steady from 20–36 months.

Table 3 shows the percentages of combined fluoride intake estimates that exceeded thresholds of 0.03, 0.04, 0.05, 0.06, and 0.07 mg F/kg bw by age. At the lower thresholds of 0.03 and 0.04, relatively consistent percentages of subjects exceeded the thresholds across all age groups. For example, the percentages exceeding 0.03 varied from 43 percent to 62 percent, with most between 57 percent and 62 percent. For higher thresholds, children were substantially more likely to exceed the threshold at ages 1.5–9 months than they were at ages 12–36 months. In general, a consistent proportion of children exceeded each threshold up to 9 months of age, and again at 20–36 months. At 12 and 16 months, however, there were lower percentages exceeding the various thresholds.

Figure 3 shows graphically the combined fluoride intake data at the individual level, using the actual ages at time of response. Substantial group variation is evident at each age. Furthermore, the lines show individual fluctuations over time by connecting results at the different ages for 10 randomly selected individuals. Individual fluctuations were generally greater over the first 12–16 months, with less variation thereafter.

The Generalized Estimating Equations (GEE) regression analyses of factors associated with fluoride intake from 1.5 to 9 months in mg F/kg bw showed (Table 4) that estimated combined fluoride intake was significantly associated with subject's age (P<.001, decrease of 0.0025 mg F/kg bw per month), mother's age (P<.001, decrease of 0.018 mg F/kg bw if the mother was aged 30 years or older), and mother's education (P<.001, decrease of 0.021 mg F/kg bw for those with some college and a decrease of 0.041 mg F/kg bw for college gradu-

TABLE 3
Percentages of Subjects with Estimated Combined Fluoride Intake Exceeding Designated Intake Levels (mg F/kg bw)

Age (Months)	Fluoride Intake Level (mg F/kg bw) 0.03	0.04	0.05	0.06	0.07
1.5	53.6	49.6	46.6	44.3	41.7
3.0	58.1	53.8	50.7	47.6	43.4
6.0	61.6	55.3	50.4	44.9	40.6
9.0	60.6	54.7	48.2	41.6	36.3
12.0	43.3	32.7	24.8	18.8	14.4
16.0	43.6	30.6	19.7	13.6	9.5
20.0	61.1	43.1	30.8	22.7	15.3
24.0	56.5	41.5	31.5	22.8	16.2
28.0	59.0	44.8	29.9	22.1	16.4
32.0	60.3	47.1	33.2	24.3	16.9
36.0	60.9	45.3	30.9	22.6	14.8

TABLE 4
Results of Regression Analyses of Factors Associated with Fluoride Intake (mg F/kg bw)

Factor	Regression Parameter Estimate	SE	P-value
1.5–9 months	0.1274	0.0086	<.0001
Intercept			
Subject's age (months)	–0.0025	0.0004	<.0001
Mother aged ≥30 years (1=yes; 0=no)	–0.0180	0.0037	<.0001
Mother a high school graduate (1=yes; 0=no)	–0.0210	0.0070	.0025
Mother a college graduate (1=yes; 0=no)	–0.0413	0.0066	<.0001
12–20 months			
Intercept	0.0363	0.0016	<.0001
Subject's age (months)	0.0005	0.0002	.0293
Subject's age^2 (months^2)	0.0004	0.0001	<.0001
Mother aged ≥30 years (1=yes; 0=no)	–0.0072	0.0018	.0001

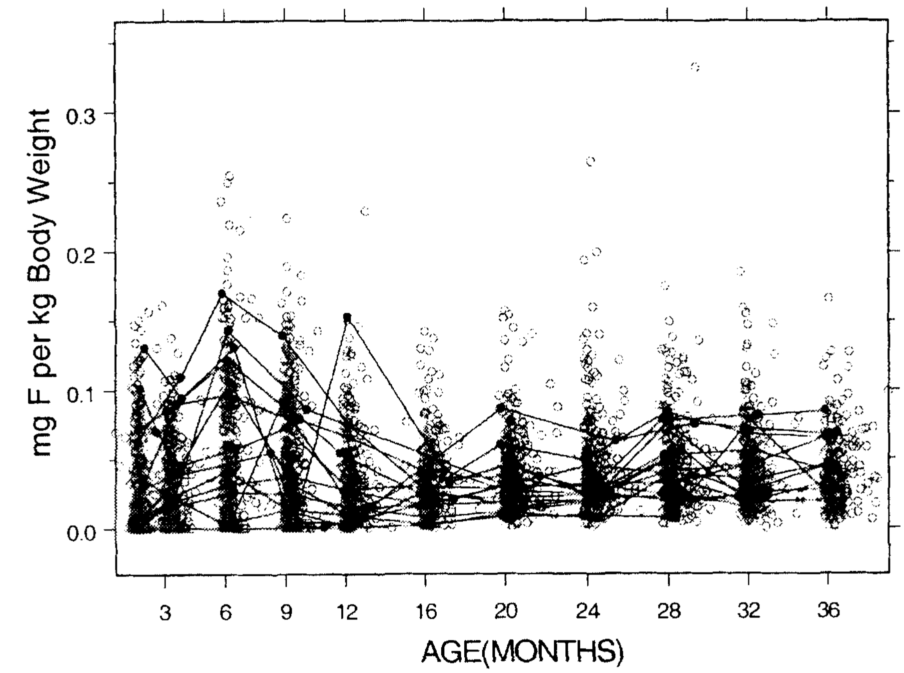
No significant variables were found for 24–36 months.

ates). Since there was evidence of a statistically significant three-way interaction among child's age, mother's age, and mother's educational level, this was investigated further by fitting a model with separate linear effects of child's age for each of the six subgroups defined by the cross-classification of mother's age and educational level. The direction of the effect of age was negative for five of the six subgroups, consistent with the main effects model displayed in Table 4. (Only for mothers aged 30 years or older with a college degree was the estimated effect of age positive.)

Estimated fluoride intake (mg per kg bw) from 12–20 months (Table 4) was related significantly to child's age (both linear and quadratic effects—coefficients of 0.0005 and 0.0004 mg F/kg bw per month, respectively) and mother's age (age 30 years or older was associated with decrease of 0.0072 mg F/kg bw). There were no other significant main effects and no significant interactions. For estimated fluoride intake per unit body weight from 24–36 months, there were no statistically significant effects of any covariates, including subjects' age.

GEE analyses with combined fluoride intake in mg (not mg F/kg bw) also were conducted, and results essentially were the same, with the addition of child's age being significant in the models for all age intervals (1.5–9 months, 12–20 months, and 24–36 months).

FIGURE 3
Patterns of Fluoride Intake per Unit Body Weight (Lines show longitudinal data for individuals.)



Discussion

The GEE methodology is useful in carrying out regression analyses of correlated data. It is particularly useful in this setting, where there are variable numbers of measurements per individual (due to missing data), and the measurements are not always collected exactly as scheduled. The methodology makes use of all available data in assessing the strength of associations between fluoride intake and relevant covariates. Since not all children participated for the full duration of the study, there is the possibility of bias due to the fact that the relationship between fluoride intake and covariates may not be the same for individuals who responded at every survey as for individuals who dropped out or who otherwise had intermittent missing values. An alternative approach for future analyses would be to estimate the missing responses using multiple imputation procedures. Such an approach is only valid if the imputation model is correct, as in any analysis. We also are working with area-under-the-curve (AUC) analyses with interpolation to summarize fluoride intake over defined periods of time.

Although very few studies have attempted to estimate fluoride intake from multiple sources simultaneously, and none have assessed longitudinal patterns of fluoride intake, it is also necessary to acknowledge that other potentially important sources of fluoride were not included in these analyses. These other sources include certain ready-to-feed foods and beverages, as well as fluoride mouthrinses, gels, and other products. The three sources that we did include (dentifrice, water, supplements) are among the most ubiquitous, generally involve relatively consistent intake patterns, and are most often identified as risk factors for dental fluorosis, so we felt they were most appropriate for analysis.

Other limitations that should be considered when interpreting the study findings: the results were by parent report without direct validation and were obtained from a single sample of predominantly white mothers of high socioeconomic status. Daily fluctuations in fluoride intake were not assessed.

The patterns of fluoride intake from the three sources were not unexpected, with water predominating early in life, largely due to many children receiving fluoridated water mixed with infant formula concentrate. Fluoride ingestion from dentifrice increased with age, generally coinciding with tooth eruption and the increasing number of teeth present. Supplement use was consistently low, on average, declining slightly with age, perhaps due to compliance issues.

In terms of combined fluoride intake on a per body-weight basis, the mean intakes appeared to be relatively stable very early in life and then again at 20 months of age and older (Figure 2), with a transitional period between about 6 and 20 months of age. This transitional period roughly coincides with estimates of the most critical ages for permanent tooth fluorosis development (1-2). Thus, it is possible that the difficulties in precisely identifying the most critical age and threshold fluoride intake levels associated with fluorosis (26) may be partially attributable to this transitional period when fluoride intakes appear to be subject to wide fluctuation. Therefore, single, cross-sectional fluoride intake estimates at a particular age (as in previous cross-sectional studies) may not be particularly valid or useful. With few studies of the relationship between fluorosis and fluoride intake in infancy, additional emphasis on this age is warranted. Although Ishii and Suckling (27) did not find dental fluorosis associated with excessive fluoride levels (7.8 ppm) up to 11 months of age, Ismail et al. (3) found a substantially elevated risk of maxillary central incisor fluorosis (OR = 5.69) for children exposed from birth or during the first year of life to greater than 2.0 ppm fluoride in the drinking water versus those exposed after age 1. Ideally, a longitudinal approach utilizing several different time points to estimate intakes and describe patterns would allow better understanding of the development of fluorosis given the dynamic nature of fluoride intake during early childhood.

In a similar vein, obtaining estimates of a threshold level of fluoride intake necessary for fluorosis development also may be inherently difficult. As evidenced by our data in Table 3, those exceeding the different thresholds at the various ages ranged from less than 10 percent to over 60 percent and varied considerably across the threshold values, particularly at the older ages. This finding is consistent with those of Rojas-Sanchez et al. (11), who found that the proportion of 28-month-olds exceeding the 0.07 mg/kg threshold for intake from food, beverages, and dentifrice varied from 18 percent to 57 percent, depending on location and fluoridation status. Clearly, these data highlight the numerous combinations of ages and intake levels that must be considered in better understanding fluorosis development.

Although this descriptive paper focused a great deal on mean fluoride intake levels and group trends, as Figure 3 demonstrates, there can often be considerable variation in individuals' fluoride intake over time. This individual variation over time also highlights the limitations involved in trying to match fluoride intake levels at an isolated (cross-sectional) time point to fluorosis development. Again, longitudinal assessment of fluoride intake appears to be critical for more thorough understanding of the complex combination of factors that may play a role in fluorosis development.

Acknowledgments

Portions of this paper were presented at the 1998 European Organization for Caries Research (ORCA) and 1999 American Association for Public Health Dentistry (AAPHD) annual meetings. This research was supported in part by grants from the National Institute of Dental and Craniofacial Research 2RO1-DE09551 and 2P30-DE10126. The authors thank Ms. Tina Craig for her assistance in manuscript preparation.

References

1. Evans RW, Stamm JW. An epidemiological estimate of the critical period during which human maxillary central incisors are most susceptible to fluorosis. J Public Health Dent 1991;51:251-9.
2. Evans RW, Darvell BW. Refining the estimate of the critical period for susceptibility of enamel fluorosis in human maxillary central incisors. J Public Health Dent 1995;55:238-49.
3. Ismail AI, Messer JG. The risk of fluorosis in students exposed to a higher than optimal concentration of fluoride in well water. J Public Health Dent 1996;56:22-7.
4. 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.
5. Singer L, Ophaug R. Total fluoride intake of infants. Pediatrics 1979;63:460-6.
6. 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.
7. 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.
8. Featherstone JDB, Shields CP. A study of fluoride intake in New York state residents. Final Report: New York State Fluoride Analysis Contract, 1988.
9. Guha-Chowdhury N, Brown RH, Shepherd MG. Fluoride intake of infants in New Zealand. J Dent Res 1990;69:1828-33.
10. 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.
11. Rojas-Sanchez F, Kelly SA, Drake KM, et al. Total fluoride intake by young children in negligibly and optimally fluoridate communities: a pilot study. Community Dent Oral Epidemiol 1999;27: 288-97.
12. Barnhart WE, Hiller LK, Leonard GJ, Michaels E. Dentifrice usage and ingestion among four age groups. J Dent Res 1974;53:1317-22.
13. Simard OL, Naccache, Lachapelle D, Brodeur JM. Ingestion of fluoride from dentifrices by children aged 12 to 24 months. Clin Pediatr 1991;30:614-17.
14. Naccache H, Simard PL, Trahan L, et al. Variability in the ingestion of toothpaste by preschool children. Caries Res 1990; 24:359-63.
15. Naccache H, Simard PL, Trahan L, et al. Factors affecting the ingestion of fluoride dentifrice by children. J Public Health Dent 1992;52:222-6.
16. Hargreaves JA, Ingram GS, Wagg BJ. A gravimetric study of the ingestion of toothpaste by children. Caries Res 1972; 6:237-43.
17. Wagener DK, Nourjah P, Horowitz A. Trends in childhood use of dental care products containing fluoride: United States, 1983-89. Advance data from Vital and Health Statistics; no 219. Hyattsville, MD: National Center for Health Statistics, 1992; pub no (PHS) 93-1250.
18. Levy SM, Kiritsy MC, Slager SL, Warren JJ. Patterns of dietary fluoride supplement use during infancy. J Public Health Dent 1998;158:228-33.
19. Levy SM, Kiritsy MC, Slager SL, Warren JJ, Kohout FJ. Patterns of fluoride dentifrice use among infants. Pediatr Dent 1997;19:50-5.
20. Warren JJ, Levy SM, Kanellis, M. Prevalence of dental fluorosis in the primary dentition. J Public Health Dent 2001;61: 87-91.
21. Levy SM, Kohout FJ, Guha-Chowdhury N, Kiritsy MC, Heilman JR, Wefel JS. Infants' fluoride intake from drinking water alone, and from water added to formula, beverages, and food. J Dent Res 1995;74:1399-407.
22. Van Winkle S, Levy SM, Kiritsy MC, Heilman JR, Wefel JS, Marshall T. Water and formula concentrations: significance for infants fed formula. Pediatr Dent 1995;17:305-10.
23. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. Biometrika 1986;73:13-22.
24. Pepe MS, Anderson GL. A cautionary note on inference for marginal regression models with longitudinal data and general correlated response data. Community Statist Simul Comput 1994;23:939-51.
25. SAS Institute. SAS/STAT user's guide. Version 6. 4th ed. Vol 2. Cary, NC: SAS Institute, Inc. 1990.
26. Bawden JW. "Where is Waldo?": the timing of fluorosis. J Public Health Dent 1996;56:5.
27. Ishii T, Suckling G. The appearance of tooth enamel in children ingesting water with a high fluoride content for a limited period during early tooth development. J Dent Res 1986;65:974-7.