Association between Enamel Hypoplasia and Dental Caries in Primary Second Molars: A Cohort Study

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Key Words

Dental caries · Enamel hypoplasia · Primary teeth

Abstract

The purpose of this study was to assess the longitudinal relationships between enamel hypoplasia and caries experience of primary second molars. The study sample was 491 subjects who received dental examinations at both age 5 and 9 by the calibrated examiners. Four primary second molars ($n = 1,892$) were scored for the presence of enamel hypoplasia for each participant. Caries presence and number of decayed and filled surfaces (dfs) were determined at age 5 and 9. The relationships between enamel hypoplasia and caries experience were assessed. Among primary second molars, 3.9% of children and 1.7% of primary second molars had enamel hypoplasia. At age 5, 36.8% of children with hypoplasia had caries, while 16.9% of children without enamel hypoplasia had caries. At age 9, the corresponding numbers were 52.6% for children with hypoplasia and 34.5% for children without hypoplasia, respectively. At the tooth level, for age 5, 28.1% of teeth with hypoplasia had caries (mean dfs = 0.40), and 7.6% of teeth without hypoplasia had caries (mean dfs = 0.11). At age 9, the corresponding numbers were 41.9% (mean dfs = 0.76) for teeth with hypoplasia and 18.3% (mean dfs = 0.34) for teeth without hypoplasia. In multivariable logistic regression analyses, teeth of subjects with enamel hy-

poplasia had a significantly higher risk for caries at age 5 and 9 after controlling for other risk factors. Enamel hypoplasia appears to be a significant risk factor for caries and should be considered in caries risk assessment.

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Developmental enamel defects are disturbances during enamel formation and may be manifested as enamel hypoplasia or opacities. Enamel hypoplasia is a quantitative defect associated with reduced thickness of enamel formed during the secretory stage of amelogenesis [Suckling, 1989; Seow, 1991]. Developmental enamel defects, such as hypoplasia, have been speculated to increase the risk of dental caries in the affected teeth [Pascoe and Seow, 1994; Li et al., 1996; Lai et al., 1997]. Defective enamel sites (hypoplasia or hypocalcification) may provide suitable local environment for adhesion and colonization of cariogenic bacteria, and bacteria may retain at the base of the defect in contact with exposed dentin, thus dental caries on these defective sites may develop more rapidly [Li et al., 1996]. Defective enamel has higher acid solubility than normal enamel and is more susceptible to caries attack [Zheng et al., 1998]. The association between enamel hypoplasia and dental caries has been reported in several cross-sectional studies [Matee et al., 1994; Pascoe and Seow, 1994; Li et al., 1996; Ellwood and O'Mullane, 1996;

Kanchanakamol et al., 1996; Milgrom et al., 2000; Montero et al., 2003; Daneshkazemi and Davari, 2005] and two longitudinal studies [Lai et al., 1997; Oliveira et al., 2006]. Enamel defects such as enamel hypoplasia appear to be a significant, reliable risk marker or predictor for dental caries; however, most of these studies were cross-sectional and did not account for other important factors, such as fluoride exposure. The duration of the two longitudinal studies collecting caries data was 36 and 52 months, respectively. Therefore, a well-designed, prospective, longitudinal study, which can take multiple important factors into consideration, is needed.

The Iowa Fluoride Study (IFS) is a longitudinal study of a cohort (from birth) concerning the relationships among fluoride exposures, biological and environmental factors, and oral health. Using data collected in the IFS on dental caries and enamel hypoplasia for primary teeth and information on important covariates, this article reports on associations between enamel hypoplasia and dental caries of primary second molars at approximately 9 years of age.

Subjects and Methods

Subjects

Children were participants in the IFS [Levy et al., 1997, 1998; Hong et al., 2004]. Newborn infants were recruited at birth between March 1992 and February 1995 from 8 Iowa hospitals, and a total of 1,390 children participated in the study. The Institutional Review Board at the University of Iowa approved all components of the IFS, and written informed consent was obtained from mothers at recruitment and again at the time of examinations. Demographic characteristics at baseline were collected and previously described [Levy et al., 1997, 1998]. Briefly, this cohort is predominantly Caucasian (about 98%), 51% girls, from families of relatively high socioeconomic status (SES, 71% having a family income of USD 30,000 or more and 46% of mothers having completed 4 years of college), 44% were first-born, 32% had been breast-fed for at least 6 months, only 4% had low birth weight and 3% had developmental disorders [Hong et al., 2004]. There were 698 subjects who received dental examinations of the primary dentition at age 5, and 603 who received second dental examinations at age 9. This report concerns a sample of 491 subjects who had participated in both dental exams at age 5 and 9 and had baseline demographic information and water fluoride assessments.

Data Collection

Parents were mailed the IFS questionnaires at 3- to 6-month intervals including a series of items concerning children's fluoride exposures and ingestion from various sources during the preceding time period or weeks. Information regarding the children's beverage intakes, breast-feeding patterns, general health/illnesses, and oral health behaviors was also obtained. Combined fluoride concentrations in water at home, school and childcare were

individually determined for each subject from public, private well, and/or bottled water sources. Daily fluoride intake (mg) was estimated from water, beverages and selected foods, dietary fluoride supplements, and fluoride dentifrice based on parents' responses to the series of questions. Parents' responses were not validated, but reliability was assessed for selected questions [Levy et al., 1997, 1998].

Dental Examinations

Dental examinations, including examination of hypoplasia and dental caries, were conducted using portable chair and halogen head light (DenLite; Welch-Allyn Medical Products, Inc., Skaneateles, N.Y., USA) at the General Clinical Research Center at the University of Iowa, or at one of several community locations by trained and calibrated dentist examiners using standardized, portable dental equipment [Slayton et al., 2001; Warren et al., 2002]. Teeth were evaluated for the presence of enamel hypoplasia using a mouth mirror and exam light, but without drying the teeth. Presence or absence of enamel hypoplasia was recorded separately for each tooth. Deficiency in enamel formation such as pits and linear grooves was recorded as enamel hypoplasia, while localized opacities that were white, yellow, or brownish in color were recorded as demarcated opacities. Enamel hypoplasia was differentiated from fluorosis [Pendrys, 1990] and other nonfluoride enamel defects using the criteria of Russell [1961]. Nonfluoride opacities are most commonly creamy-yellow to brown in color, well demarcated, and on the smooth surfaces. Fluorosis is more symmetrical and more diffuse, with white striations or patches that do not have well-defined margins [Slayton et al., 2001].

Children's Dental Caries Experience

For the dental caries examinations, halogen headlights were used, teeth were dried, and the DenLite mirror system provided additional lighting to augment the primarily visual examination, but a dental explorer was used to confirm questionable caries findings. A modified D₁-D₃ version of the criteria of Pitts and Fyffe [1988], Pitts [1997] and Ismail et al. [1992] was used to record caries lesions in this study. Our criteria [Warren et al., 2002] combined cavitated enamel (d₂) and dentin (d₃) lesions into a single d₂₋₃ category that was distinguished from d₁ (noncavitated) lesions. For this report, caries experience was considered in two ways. First, caries presence was defined as having any decayed (cavitated d₂₋₃ lesions) and/or filled surfaces on primary second molars (yes/no). Second, the number of decayed (cavitated d₂₋₃ lesions) and/or filled surfaces (dfs) was calculated on primary second molars. These caries measures were calculated for both age 5 and 9 exams. Caries incidence was computed as the percentage of subjects with new caries, and caries increments as increases in d₂₋₃fs; d₁ lesions were not used for these analyses. Teeth with a dental sealant were excluded from all analysis.

All examinations were done by one of three trained and calibrated dentist examiners, with calibration sessions scheduled before and midway through each set of exams. A small percentage of subjects was used for duplicate examinations to assess interexaminer reliability. All teeth were examined for both hypoplasia and caries, but only primary second molars were used for these analyses, since they were most consistently present for both examinations at age 5 and 9. Person-level hypoplasia and caries were defined as present whenever any of the primary second molars exhibited hypoplasia or caries.

Statistical Analysis

Descriptive statistics were generated for caries experience by enamel hypoplasia status. Bivariate analysis was conducted at both the person and tooth levels. At the person level, children were classified into two mutually exclusive groups: with and without hypoplasia. Using the no-hypoplasia group as the reference, caries in children with enamel hypoplasia (both prevalence and d_{2-3fs}) was compared at age 5 and 9 using the χ^2 test for prevalence and the Wilcoxon two-sample test for d_{2-3fs} . Caries increase from age 5 to 9 (percent incidence and d_{2-3fs} increment) was also compared. Bivariate analyses at the tooth level were conducted using generalized log-linear models (to compensate for intrasubject correlations) for caries presence and generalized linear models with negative binomial distribution for d_{2-3fs} .

Multivariable regression models were developed for caries at the tooth level using enamel hypoplasia as the explanatory factor, after controlling for other potentially important factors. These other potential predictors included gender, childhood illness (yes/no), gestational weeks, birth weight, breast-feeding for 6 months or more (yes/no), SES [Shenkin et al., 2004], fluoride concentration of home drinking water (tap, well, and/or bottled), average daily fluoride intake, average daily soda pop intake, daily toothbrushing frequency, and previous (age 5) d_{2-3fs} (for age 5–9 increment models only). Three levels of SES were defined: (1) low – families with less than USD 30,000 income per year and in which mothers did not have a 4-year college degree; (2) middle – families with an annual income of USD 30,000–49,999, but excluding those with mothers having a graduate or professional degree, or less than USD 30,000 but having mothers with a 4-year college or graduate/professional degree; (3) high – mothers with a graduate/professional degree and USD 30,000 or more annual family income or USD 50,000 or more income regardless of the mother's educational level.

For these other potential predictors, bivariate associations with caries at age 5 and 9 were assessed using simple logistic regression for prevalence data (percentage of subjects with caries) and Spearman correlations for count data (d_{2-3fs}) at the person level (not tooth level). Those variables that were significant at $\alpha = 0.10$ were used in backward elimination multivariable models, and the final model included variables that were jointly significant at $\alpha = 0.05$, plus hypoplasia. Because caries data for individual teeth within the same subject are correlated, statistical methods must account for the correlation between teeth within a subject. A subject-level hypoplasia score was defined as the mean number of primary second molars with hypoplasia and was used to assess between-subject effects of hypoplasia. A within-subject hypoplasia score for each tooth was also defined using contrasts between tooth-level scores (0.1) and person-level averages. For example, a subject having one tooth with hypoplasia (out of 4) would have four within-subject hypoplasia scores (0.75, –0.25, –0.25, and –0.25). Use of the within-subject hypoplasia score in regression models gives insight into differences between hypoplastic teeth vs. nonhypoplastic teeth within the same subject [Mancl et al., 2000]. Logistic generalized estimating equation models (GEE) [Evans and Li, 2005] were used for binary outcomes (yes/no), and negative binomial GEE models for count outcomes (d_{2-3fs}). All statistical tests were conducted using SAS 9.1 for Windows, with p values below 0.05 being considered as statistically significant.

Results

Interexaminer reliability was assessed from duplicate examinations. Weighted kappa for person-level d_{2-3fs} was 0.90 at age 5 and 0.90 at age 9. For enamel hypoplasia, person-level kappa was 1.0 at age 5.

Considering the primary second molars of 491 children, 3.9% of children had hypoplasia, 17.7% of children had caries at age 5, 35.2% had caries at age 9, and 31.1% developed new carious lesions from age 5 to 9. Table 1 shows that at the tooth level, 1.7% of all primary second molars had hypoplasia. Among all 1,892 primary second molars included in the analyses, 7.9% had caries at age 5 (mean $d_{2-3fs} = 0.11$ per tooth), 18.7% at age 9 (mean $d_{2-3fs} = 0.34$ per tooth), and 14.5% had an increase in caries from age 5 to 9. Caries distributions for individual molars (A, J, K, T: FDI 55, 65, 75, 85) are also included in table 1.

The bivariate relationships between enamel hypoplasia (age 5 exam) and caries experience of primary second molars at ages 5 and 9, and incidence from age 5 to 9 are presented in table 2. Children with enamel hypoplasia had more caries than those without enamel hypoplasia for both prevalence/presence and d_{2-3fs} at both ages 5 and 9 at both the person and tooth levels. The bivariate association was statistically significant for caries at age 5 for both person and tooth levels, even though there were only 19 children with hypoplasia. For example, at the person level, 36.8% of children with hypoplasia had caries at age 5 vs. only 16.9% of children without enamel hypoplasia (relative risk, $RR = 2.17$). With larger sample sizes in the tooth level analyses, teeth with enamel hypoplasia had significantly more caries at age 9 ($RR = 1.75$, $p < 0.01$). However, while caries increment from age 5 to 9 was elevated for subjects with hypoplasia, caries was not significantly related to enamel hypoplasia at either the person or tooth level ($RR = 1.55$ for each).

Screening for other important potential predictors for caries levels (yes/no at age 5, age 9 and age 5–9 increment) used simple logistic regression (at the person level) and examined bivariate associations with gender, age, childhood illness, gestational age, birth weight, breast-feeding (<6 months vs. ≥ 6 months), SES (three levels), fluoride concentration of home drinking water, average daily fluoride intake (mg), average daily soda pop intake (oz) and daily toothbrushing frequency. Spearman correlations were used to examine the bivariate associations of these same potential risk factors with caries counts (d_{2-3fs}) for age 5, age 9 and age 5–9 increments. Variables having associations with $p < 0.10$ are listed in the foot-

Table 1. Distribution of enamel hypoplasia, dental caries in primary second molars and subject-level factors

	Tooth A (FDI 55)	Tooth J (FDI 65)	Tooth K (FDI 75)	Tooth T (FDI 85)	All second molars (n = 1,892) ^a
Enamel hypoplasia prevalence, %	1.5	1.1	2.1	2.1	1.7
<i>d</i> _{2-3fs}					
Prevalence, %					
Age 5	8.4	7.2	9.1	7.0	7.9
Age 9	20.4	19.4	17.3	17.7	18.7
Incidence, %					
Age 5–9	16.2	16.0	13.0	13.0	14.5
Incidence, mean ± SD					
Age 5	0.11 ± 0.38	0.10 ± 0.42	0.11 ± 0.38	0.10 ± 0.42	0.11 ± 0.40
Age 9	0.39 ± 0.86	0.37 ± 0.83	0.32 ± 0.84	0.28 ± 0.71	0.34 ± 0.82
Increment	0.29 ± 0.74	0.28 ± 0.71	0.22 ± 0.67	0.19 ± 0.56	0.25 ± 0.67
Subject-level factor	Prevalence, %		p value ^b		
	subjects without hypoplasia	subjects with hypoplasia			
Gender					
Boys	49	53			0.76
Girls	51	47			
SES					
Low	22	6			0.13
Middle	36	56			
High	43	39			
Childhood illness	25	37			0.25
Breast-fed 6 months or more	32	39			0.52
	mean ± SD	mean ± SD	p value ^c		
Gestational weeks	39.5 ± 2.1	40.3 ± 1.2			0.01
Birth weight, kg	3.5 ± 0.6	3.6 ± 0.3			0.15
Dental exam age, years					
Primary dentition exam 1	5.1 ± 0.4	5.1 ± 0.3			0.56
Mixed dentition exam 2	9.2 ± 0.7	9.2 ± 0.8			0.95
Age increment (exam 1–2)	4.1 ± 0.7	4.2 ± 0.8			0.71
Home tap fluoride, ppm					
Age 3–5	0.83 ± 0.45	0.67 ± 0.45			0.11
Age 6–9	0.81 ± 0.43	0.64 ± 0.45			0.09
Daily fluoride intake, mg					
Age 3–5	0.77 ± 0.37	0.72 ± 0.33			0.55
Age 6–9	0.72 ± 0.35	0.56 ± 0.22			0.43
Daily soda pop intake, oz					
Age 3–5	2.2 ± 2.1	1.7 ± 2.3			0.32
Age 6–9	3.0 ± 2.4	2.9 ± 2.7			0.87
Daily toothbrushing frequency					
Age 3–5	1.3 ± 0.5	1.5 ± 0.5			0.14
Age 6–9	1.5 ± 0.5	1.7 ± 0.5			0.15

^a Mean *d*_{2-3fs} (SD) is per tooth. Some teeth were excluded due to presence of sealants. ^b p value from χ^2 test. ^c p value from t test.

Table 2. Bivariate associations between dental caries and enamel hypoplasia of primary second molars

Person level (per person)	n	d ₂₋₃ f prevalence	Relative risk (95% CI)	p value ^a	d ₂₋₃ fs count					p value ^b
					0	1	2	3	4+	
Caries prevalence at age 5										
Without hypoplasia	472	16.9%	reference	0.03	392	29	19	12	20	0.03
With hypoplasia	19	36.8%	2.17 (1.17 to 4.05)		12	3	1	1	2	
Caries prevalence at age 9										
Without hypoplasia	469	34.5%	reference	0.11	307	36	37	19	70	0.07
With hypoplasia	19	52.6%	1.52 (0.98 to 2.38)		9	1	2	1	6	
Caries increment (age 5–9)										
Without hypoplasia	469	30.5%	reference	0.12	326	39	30	21	53	0.15
With hypoplasia	19	47.4%	1.55 (0.95 to 2.54)		10	3	3	0	3	

Tooth level (per tooth)	n	d ₂₋₃ f prevalence	Relative risk ^c (95% CI)	p value ^c	Estimated d ₂₋₃ fs ^d (95% CI)	p value ^d
Caries prevalence at age 5						
Without hypoplasia	1,849	7.6%	reference	<0.01	0.11 (0.08 to 0.14)	<0.01
With hypoplasia	32	28.1%	3.11 (1.69 to 5.73)		0.40 (0.21 to 0.75)	
Caries prevalence at age 9						
Without hypoplasia	1,831	18.3%	reference	0.02	0.34 (0.29 to 0.41)	<0.01
With hypoplasia	31	41.9%	1.75 (1.11 to 2.74)		0.76 (0.46 to 1.26)	
Caries increment (age 5–9)						
Without hypoplasia	1,831	14.4%	reference	0.16	0.25 (0.21 to 0.30)	0.06
With hypoplasia	31	25.8%	1.55 (0.84 to 2.85)		0.46 (0.25 to 0.87)	

^a p value from χ^2 test. ^b p value from Wilcoxon two-sample test for d₂₋₃fs. ^c Relative risk and p values from generalized log-linear models. ^d Estimated d₂₋₃fs, CI and p values from generalized linear models with negative binomial distribution.

notes to tables 3 and 4, and were used in backward elimination GEE procedures.

Final GEE models for caries presence/incidence and counts/increments included all variables that remained jointly significant ($p < 0.05$), plus hypoplasia, and are detailed in tables 3 and 4, respectively. The tooth level data ($n = 1,892$) needed to compensate for intrasubject correlation and hence the tooth-level multivariable models used GEE methods. Logistic GEE models predicting caries (yes/no) at age 5 and 9, and any new caries from age 5 to 9, were fitted using the aforementioned selected predictors, along with hypoplasia, and final models are presented in table 3. The models were developed for repeated-measures or clustered data. After controlling for the other important predictor variables, children with enamel hypoplasia had a significantly higher risk of caries (see ‘between-subject’ hypoplasia variable) at both age 5 (odds ratio, OR = 7.56, $p < 0.01$) and age 9 (OR = 5.16, $p = 0.03$), but no significant association with caries incidence (OR = 1.02, $p = 0.97$). Within-subject hypoplasia was not a sig-

nificant factor in any of the models, indicating that, for a given subject, the caries risk for hypoplastic and nonhypoplastic teeth was comparable.

Repeated-measures negative binomial GEE models were constructed to predict the number of decayed and filled surfaces (d₂₋₃fs) at age 5, age 9 and age 5–9 d₂₋₃fs increment (table 4). Between-subject hypoplasia was a statistically significant predictor for d₂₋₃fs at age 5 (parameter estimate = 1.89, $p < 0.01$), age 9 (parameter estimate = 1.39, $p < 0.01$), and age 5–9 caries increment (parameter estimate = 1.28, $p = 0.04$). Within subjects, there was a significant increase in age 5 d₂₋₃fs associated with teeth exhibiting hypoplasia (parameter estimate = 1.46, $p = 0.03$) and age 9 d₂₋₃fs (parameter estimate = 0.90, $p = 0.03$), but not age 5–9 d₂₋₃fs increment (parameter estimate = 0.70, $p = 0.19$). It is noteworthy that all d₂₋₃fs estimates were higher, both for subjects with more hypoplasia and for teeth exhibiting hypoplasia throughout the analyses, even though some were not statistically significant.

Table 3. Tooth level logistic GEE models for caries (yes/no) using backward elimination method

Tooth outcome	Predictor variables	Odds ratio unit ^a	Odds ratio (95% CI)	p value
Caries presence (yes/no) at age 5 ^c	between-subject hypoplasia ^b	all second molars (vs. none)	7.56 (2.28–25.07)	<0.01
	within-subject hypoplasia ^b	1 tooth more than subject average	2.80 (0.88–8.95)	0.08
	dental exam age, years	1 year	1.91 (1.11–3.28)	0.02
	breast-feeding	<6 months (vs. ≥6 months)	2.15 (1.16–3.98)	0.01
	average home tap water fluoride concentration (3–5 years of age)	1.0 ppm	2.36 (1.29–4.30)	<0.01
Caries presence (yes/no) at age 9 ^d	between-subject hypoplasia ^b	all second molars (vs. none)	5.16 (1.15–23.14)	0.03
	within-subject hypoplasia ^b	1 tooth more than subject average	1.61 (0.68–3.81)	0.27
	average daily fluoride intake during 5–9 years of age	1 mg F per day	1.90 (1.05–3.42)	0.03
	average daily toothbrushing frequency during 5–9 years old	one more time per day	2.16 (1.49–3.09)	<0.01
Caries incidence (yes/no) age 5–9 ^e	between-subject hypoplasia ^b	all second molars (vs. none)	1.02 (0.31–3.39)	0.97
	within-subject hypoplasia ^b	1 tooth more than subject average	1.73 (0.40–7.57)	0.47
	previous caries (age 5)	1 d ₂₋₃ fs	5.08 (3.48–7.42)	<0.01
	average daily fluoride intake during 5–9 years of age	1 mg F per day	1.90 (1.01–3.59)	0.048
	average daily toothbrushing frequency during 5–9 years old	one more time per day	1.97 (1.36–2.85)	<0.01

^a Odds ratios represent the change in odds relative to 1 unit change in the predictor variable.

^b The 'between-subject' hypoplasia variable addresses differences between subjects with and without hypoplasia, and the 'within-subject' hypoplasia variable addresses differences within subjects (for subjects having hypoplasia) between teeth with hypoplasia and teeth without hypoplasia.

^c Additional variables included for consideration were: age 3–5 averages for estimated daily fluoride intake (mg F), estimated soda pop intake (oz) and daily tooth brushing frequency.

^d One additional variable was included for consideration: age 5–9 average estimated soda pop intake (oz).

^e Additional variables included for consideration were: previous (age 5) d₂₋₃fs, and age 5–9 average estimated soda pop intake (oz).

Table 4. Tooth level negative binomial GEE models of caries d₂₋₃fs counts and important predictor variables using backward elimination

Outcome	Predictor variables	Unit ^a	Parameter estimate (95% CI)	p value
Number of decayed or filled surfaces at age 5 (d ₂₋₃ fs) ^c	between-subject hypoplasia ^b	all second molars (vs. none)	1.89 (0.72–3.06)	<0.01
	within-subject hypoplasia ^b	1 tooth more than subject average	1.46 (0.14–2.79)	0.03
	age at dental examination, years	1 year	0.62 (0.22–1.03)	<0.01
	average home tap water fluoride concentration (3–5 years of age)	1 ppm	1.09 (0.51–1.68)	<0.01
	average daily soda pop intake during 3–5 years of age	1 oz	0.08 (0.01–0.15)	0.03
Number of decayed or filled surfaces (dfs) at age 9 ^d	between-subject hypoplasia ^b	all second molars (vs. none)	1.39 (0.50–2.29)	<0.01
	within-subject hypoplasia ^b	1 tooth more than subject average	0.90 (0.12–1.68)	0.03
	age at dental examination, years	1 year	0.27 (0.04–0.50)	0.03
	average daily fluoride intake during 5–9 years of age	1 mg F per day	0.65 (0.08–1.23)	0.03
	average daily toothbrushing frequency during 5–9 years old	one more time per day	0.70 (0.34–1.06)	<0.01
d ₂₋₃ fs increment (number of new d ₂₋₃ fs) age 5–9 ^e	between-subject hypoplasia ^b	all second molars (vs. none)	1.28 (0.11–2.45)	0.04
	within-subject hypoplasia ^b	1 tooth more than subject average	0.70 (0.33–1.74)	0.19
	age 5 d ₂₋₃ fs	1 d ₂₋₃ fs	0.14 (0.11–0.17)	<0.01
	average daily toothbrushing frequency during 5–9 years old	one more time per day	0.72 (0.38–1.06)	<0.01

^a The parameter estimate represents the change in estimated d₂₋₃fs relative to 1 unit change in the predictor variable.

^b The 'between-subject' hypoplasia variable addresses differences between subjects with and without hypoplasia, and the 'within-subject' hypoplasia variable addresses differences within subjects (for subjects having hypoplasia) between teeth with hypoplasia and teeth without hypoplasia.

^c One additional variable was included for consideration: breast-fed 6 months or more (yes/no).

^d Additional variables included for consideration were: sex, SES, and age 5–9 average estimated soda pop intake (oz).

^e Additional variables included for consideration were: childhood illness, SES, and age 5–9 average estimated daily fluoride intake (mg F).

Discussion

This prospective study examined the risk of dental caries on primary second molars associated with enamel hypoplasia in a cohort of children from birth to age 9. The primary second molars were the teeth most consistently present at both examinations, and limiting to this tooth type helped to reduce the confounding effects of differential caries rates on different tooth types (canines had much lower caries rates). Therefore, although some of the total caries experience would be missed due to many primary teeth not being included, the confounding effect of differing caries rates would be avoided.

The results of the bivariate analyses indicated that enamel hypoplasia was significantly associated with dental caries. The trend was generally consistent at all levels of bivariate analysis, at both the person and tooth levels, for age 5 findings, and to a lesser degree for age 9 and age 5–9 incidence. However, results were not consistently significant. Theoretically, from the view of pathogenesis, teeth with enamel hypoplasia should have a higher risk of dental caries because hypoplastic enamel surfaces have reduced thickness of enamel and may provide a more suitable local environment for adhesion and colonization of cariogenic bacteria [Li et al., 1996], and are more acid-soluble [Zheng et al., 1998].

The results were somewhat consistent with previous studies, which suggested that enamel defects increase the risk of dental caries in the affected teeth [Pascoe and Seow, 1994; Li et al., 1996; Lai et al., 1997; Milgrom et al., 2000; Montero et al., 2003; Oliveira et al., 2006]. From the results of multivariable regression analyses, the between-subject effect from enamel hypoplasia was consistently significant except for age 5–9 incidence (table 3). This indicates that subjects with hypoplasia are more at risk for caries at age 5 and 9, and also likely to have more surfaces affected by caries (table 4). It should be noted, however, that most of the caries in the study was treated (i.e. 'filled'), so that some dentists' decisions to preferentially treat hypoplastic teeth at an earlier age may also partially explain these findings.

However, the within-subject effect from enamel hypoplasia was not consistently significant. This might suggest that, for subjects exhibiting enamel hypoplasia, the risk for developing caries is similar for all teeth. Also, the weaker effects of hypoplasia on caries increments may indicate that hypoplasia has a stronger early influence (seen in age 5 caries experience, with a carryover effect on age 9 caries experience), but that the effect may not continue to put subjects at an increased risk for caries many years after eruption.

Despite the dramatic decline in dental caries experience in the last several decades in the US and some other developed countries, dental caries remains a significant health problem [National Institute of Health, 2000]. Extensive evidence indicates that dental caries is a communicable infectious disease [Caufield, 2005], which involves many environmental and host factors and the interactions among these factors [Featherstone, 1990, 2000; Fejerskov and Kidd, 2003]. This supports a paradigm shift from a surgical model which focuses mainly on removing the carious tooth structure followed by replacement with a restorative material to a biological/medical model in which the individual's overall and site-specific susceptibility are assessed and interventions can be individualized to prevent and control this infection [Horowitz, 2004]. Therefore, in contemporary management of dental caries with this medical model, caries risk assessment plays a crucial role [Powell, 1998; Reich et al., 1999; Hausen, 2003; Fontana and Zero, 2006; American Dental Association, 2009]. Unfortunately, there is no simple, valid, and reliable caries risk assessment model currently available. Previous caries experience and/or untreated (active) lesions are the best predictors for future caries development [Bibby and Shern, 1978; Disney et al., 1992; Leverett et al., 1993; Hausen et al., 1994; Vanobbergen et al., 2001; Featherstone et al., 2003]. However, these predictors are post-disease and do not serve well for early detection and primary prevention of the disease. As a result, they might not be as useful to a practitioner trying to control and prevent caries at the earliest stages in susceptible patients. In this study, after controlling for other potential factors, multivariable regression models suggested that enamel hypoplasia seems to be a good predictor. Enamel hypoplasia might not only itself render the tooth more prone to caries development, but also be in part a proxy indicator for substandard nutrition and/or childhood infection. All of these negative early life experiences during enamel formation might manifest collectively as enamel hypoplasia. These sorts of events will put a child at higher risk for dental caries. Together with other information, such as fluoride concentration of home water source, other fluoride exposures, soda pop intake, and brushing frequency, a risk assessment model that considers enamel hypoplasia data could provide good prediction of early caries risk, particularly at the tooth level. Enamel hypoplasia might have good potential to serve as a predictor of caries experience, because the teeth could be examined for hypoplasia right after eruption, before carious lesions develop. Thus, early intervention measures could be applied with at-risk children to prevent early caries stages.

The results from this study indicate that enamel hypoplasia is a significant predictor for dental caries of childhood. However, several limitations of the study must be recognized. Several important factors related to dental caries, such as oral bacteria and plaque levels, were not included in the analysis. The subjects were mostly Caucasian and from families with relatively high SES in Iowa. Such a convenience sample limits the generalizability of the results to other groups of children. In addition, the number of children who were diagnosed with hypoplasia (only 19) was small and a small change in diagnosis reliability could have an impact on the results. Within the study limitations, this prospective, longitudinal study of the birth cohort provided evidence that enamel hypoplasia

could be a clinically meaningful predictor for dental caries. More studies are needed to better understand the role of enamel hypoplasia in caries development, including studies of longer duration, with larger, more diverse samples, and assessing other important factors related to dental caries. Also, studies are needed to understand the factors related to the time-dependent effects of enamel hypoplasia on caries presence at age 5 and 9.

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