Antecedents and correlates of hypoplastic enamel defects of primary incisors

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Abstract

Four hundred and fifty-five exfoliated primary incisors were obtained from children whose mothers provided information about a wide range of pre-, peri-, and postnatal characteristics of both the mother and child. These teeth then were examined for the presence of hypoplastic enamel defects (HED). The basic form of the null hypothesis tested was that children who had HED of a primary incisor did not differ from those who did not have such a defect. Of the primary incisors examined, 18.5% had HED (25.0% maxillary and 10.1% mandibular). The following items were found to be associated most strongly ($P < 0.003$) with an increase in a child's risk of developing HED; 1) maternal antenatal history of smoking, higher prepregnancy weight, and failure to obtain prenatal care during the first trimester; 2) prematurity, low birth-weight and their associated correlates; and 3) postnatal measles infection. Left-handedness, maternal tea and Tylenol (McNeil Consumer Products Co., Fort Washington, PA) consumption, and failure to screen for undue lead burden were associated less prominently ($P < 0.05$) with HED prevalence. Season of birth and serum and dentin lead levels were not related to the prevalence of HED. Many of these risk factors are also covariates of low socioeconomic status such as suboptimal nutrition and increased risk of infection. Additional investigation is needed to delineate the associations between specific pre- and perinatal nutritional and infectious factors, socioeconomic status, and HED development. (Pediatr Dent 14:158–66, 1992)

Introduction

Enamel formation of the primary incisors begins at approximately 14 weeks in utero and is complete by the end of the third postnatal month.[1] Because enamel is a relatively stable structure, defects involving matrix secretion and/or maturation of the enamel of the primary incisors can act as a permanent record of insults occurring pre-, peri-, or early postnatally. Even the normal physiological event of birth is recorded in the enamel and dentin of primary teeth as the neonatal line.[2]

Enamel defects of the human primary dentition have been reported to occur in 5.9 to 33.0% of "normal" children[3–7] and in up to 77.0% of children from "underdeveloped" countries or populations.[8–17] These defects have been associated with a multitude of systemic exposures, disturbances, and illnesses.[18–21] The literature abounds with studies investigating the correlates or antecedents of hypoplastic defects of the primary dentition (Table 1, next page). These can be categorized as allergic, chemical, infectious, metabolic, neurologic, nutritional, or perinatal (prematurity/low birth-weight, hypocalcemia, respiratory distress or asphyxia) in origin. Unfortunately, many of these studies are of limited value because of selection bias, highly variable quality of exposure information, and lack of controls.

Exfoliated primary incisors were collected from children who were followed from shortly after birth, when their mothers were interviewed about pregnancy and demographic characteristics. This provided a unique opportunity to identify antecedents or correlates of hypoplastic enamel defects (HED) of primary incisors from this sample of "normal" children. Our findings prompted us to seek unified hypotheses that account for the development of these defects.

Materials and Methods

One exfoliated primary incisor, free of caries, restorations, or missing enamel, was collected from each of 455 children born in one hospital between April 1, 1979 and March 31, 1980. Recruited for an epidemiologic study of the effects of low-level lead exposure, parents of 1982 children mailed primary teeth for dentin lead level analysis. The last 670 teeth received were included in the present study. Two hundred and fifteen teeth were not evaluated because of: l) damage during mailing; 2) the presence of caries; 3) the presence of restorations; 4) significant portions of missing enamel due to fracture of the desiccated tooth; or 5) not being identified as a primary incisor. More than half (61.6%) of the children were born to mothers who completed 16 years of formal education, and less than 4% of families received public assistance. Only 4.9% of the children were born before the 37th week of gestation.

Mothers were interviewed during the first and second postnatal day to obtain information about demographic characteristics, their reproductive and medical history, as well as about exposures during pregnancy.[22–24] Medical records were reviewed to obtain information about the newborn, and about events during pregnancy

Table 1. Systemic exposures, disturbances, or illnesses associated with defects of the primary dentition

Allergic[73]
Chemical
Fluoride [74,75,76,77]
Tetracycline[78,70]
Thalidomide[80]
Infectious
Viral[81,82,83,84]
Bacterial[85,10]
Metabolic
Diabetes[86,87,88,89]
Hypocalcemia[46,47,39]
Hypothyroidism[90,91,92]
Gastrointestinal malabsorption[93,94]
Neurological[95,96,97,98,99,100,101,69,102,103]
Nutritional[12]
Vitamin A deficiency[10]
Vitamin D deficiency[104,105,106,35]
Perinatal Disturbances
Prematurity/low birth weight[107,108,109,110,111,112,113,100,88,114,48,115,68,39,116,117,118,119,120]
Hypocalcemia[34,35,36,37,38,39,40]
Respiratory disturbances[121,122,123,68]

and delivery. Lead content of umbilical cord blood was measured at birth in duplicate by anodic-stripping voltammetry to a precision of 2 μg/dL.[25] When the child was approximately 6 years old, the family was mailed a questionnaire about changes in demographic variables, early child care arrangements, and the child's medical history since birth. Also sent was a two dollar bill ("from the tooth fairy") and a request to return one of the child's exfoliated primary teeth in the container provided. If more than one exfoliated primary incisor was received, only the first tooth received was evaluated for HED. Prior to destruction for analysis of dentin lead levels, the teeth were prepared for visual examination by cleaning the outer surfaces with dental scalers and a standard dental prophylaxis cup on a slow-speed handpiece using lead-free flour of pumice. All teeth were dried and examined by the principal author (HLN) using a 4x magnifying loop under direct illumination. Intraobserver reliability was tested by having the examiner randomly and blindly reevaluate 123 of the sample teeth at different sessions. The Kappa Score for identification of hypoplastic defects was 0.66, which is comparable to that of other diagnostic procedures.[26]

The type and location of each tooth were identified. Defects were recorded using the DDE Index, an epidemiological index of developmental defects of dental enamel developed by the Commission on Oral Health, Research and Epidemiology of the Federation Dentaire Internationale.[27] For this study, hypoplastic pits and grooves were combined into one category of defect — hypoplastic enamel defects (HED). Because hypoplasia is considered to be the type of enamel defect most likely to result from a systemic insult, HED is the only enamel defect evaluated in this study.

The lead levels of the teeth were measured by anodic-stripping voltammetry in two specimens of central dentin proximal to the cementoenamel junction. The lead values were averaged if they differed by 2.5 μg/g or less. Otherwise, two additional specimens were analyzed, and the three closest values averaged.[28]

The basic form of the null hypothesis tested was that children who had HED of a primary incisor did not differ in their distribution of exposures and characteristics from children who did not have such a defect. Chi-square statistics were calculated for dichotomous variables and *t*-statistics for continuous variables after normalization by log transformation if necessary.

Results

Of the 455 primary incisors evaluated, 18.5% had HED (25.0% maxillary and 10.1% mandibular). A complete description and analysis of these teeth and the various types of macroscopic enamel defects detected have been reported previously.[7] Fully 42.1% of the infants who were premature (< 37 weeks, N = 19) and 40.9% of the infants whose birth-weights were less than 2500 g (N = 22) had HED, compared with 17.6% for full-term babies (N = 433) and 17.4% for infants weighing more than 2500 g (N = 430, Table 2, next page). Gestational age and birth-weight were not available for three of the infants.

Of the 118 variables that characterize the mother's medical and reproductive history, the pregnancy, the delivery, and the baby's well-being during the neonatal period, several demonstrated a significantly different distribution between children who had HED and those who did not (Tables 3, page 161, and 4, page 162). Children were at increased risk for HED if their mothers: 1) consumed three or more cups of tea daily during the first trimester ($P = 0.03$); 2) took Tylenol (McNeil Consumer Products Co., Fort Washington, PA) during the pregnancy ($P = 0.04$); and 3) had a greater prepregnancy weight (P 0.0001). The risk of HED also increased in babies born to mothers who first presented for prenatal care after the first trimester ($P = 0.007$). Although mean years of maternal smoking were significantly higher for children with HED than for those without HED ($P = 0.0008$), the proportion of mothers who identified themselves as "current smokers" shortly

Table 2.
Prevalences of enamel defects of primary teeth in premature, low birthweight infants

Source	Sample		Percentage of Children Affected		
	N	Criteria	Hypoplasia	Opacity	Total
Stein (1947)	16	<7th month GA			50.0
	>200	AGA			< 1.0
Forrester & Miller (1955)	99	P			56.6
Miller & Forrester (1959)	109	AGA			3.7
Grahnen & Larsson (1958)	68	< 3000 gms			32.4
	61	> 3000 gms			13.1
Rosenwieg & Sahar (1962)	21	< 2300 gms	23.8		
	80	> 2300 gms	1.2		
Grahnen *et al* (1972)	26	SGA, normal length			0.0
	26	SGA, short			19.2
	26	Dysmature			11.5
	56	AGA, normal weight			12.5
Grahnen *et al* (1974)	82	< 38 wks	21.9	20.7	42.6 *
	39	AGA	5.1	10.3	15.4 *
Rosenstein (1974)	64	P & < 2000 gms	26.6	18.7	45.3
Funakoshi *et al* (1981)	20	SGA	20.0		
	32	AGA	34.4		
	29	< 34 wks	41.4 *		
	23	> 34 wks	13.0 *		
Mellander *et al* (1982)	91	< 2000 gms	20.9	12.1	33.0
	48	AGA	16.7	22.9	39.6
	53	PAGA			37.7 *
	25	PSGA			16.0 *
	13	AGA & SGA			23.1 *
Johnson *et al* (1984)	67	< 1500 gms	20.8	31.4	52.2 *
	46	AGA	4.3	21.7	26.0 *
Noren *et al* (1984)[39]	91	< 2000 gms	17.6	12.1	29.7
	48	FAGA	16.7	22.9	39.6
Seow *et al* (1984)	63	< 1500 gms			60.3
Pimlott *et al* (1985)	106	< 37 wks & <1500 gms	37.0		
Seow *et al* (1987)	77	< 1500 gms	51.9	10.4	62.3 * * *
	33	1500 - 2500 gms	21.2	6.1	27.3 * *
	47	> 2500 gms	6.4	6.4	12.7
Seow *et al* (1989)	45	1149 ±191gms, 29.4 ±2.3wks			68.9
Fearne *et al* (1990)	110	< 2000 gms	71.0 *	22.0	77.0 * ‡
	93	> 2000 gms	15.0 *	27.0	37.0 * ‡
Needleman *et al* (1991)	19	< 37 wks	42.1 *		
	433	> 37 wks	17.6 *		
	22	< 2500 gms	40.9 *		
	430	> 2500 gms	17.4 *		

A — Appropriate *GA — Gestational Age* *H — Hypoplasia* *S — Small*
F — Full Term *gms — Grams* *P — Preterm* *wks — Weeks*

* p< 0.05, ‡ totals represent the number of *teeth* observed with hypoplasia and/or opacity defects

Table 3. The percentage of children whose tooth did or did not have a HED who also had the characteristic listed on the left

	Hypoplastic Enamel Defects		
	Yes	*No*	*P value*
Prenatal			
Alcohol consumption (any)	42.9	38.9	.90
Coffee consumption (3+ cups) 1st trimester	19.1	17.9	.82
Maternal diabetes	15.5	14.1	1.00
Prenatal care began > 1st trimester	11.3	5.0	.007
Sexually transmitted disease	22.6	16.8	.84
Tea consumption (3+ cups) 1st trimester	15.5	7.3	.02
Tylenol use	22.6	13.6	.04
Urinary tract infection	19.1	16.6	.46
Perinatal			
Pitocin augmentation	25.0	40.8	.009
Premature labor	8.3	1.6	.004
Prematurity	9.5	3.0	.0001
Special care nursery	27.4	14.1	.005
Postnatal			
Hearing problem	0.0	18.7	.08
Left-handedness	16.2	6.3	.01
Measles infection	11.4	0.9	.00008
No lead screening	24.3	38.2	.03

after delivery was not significantly elevated ($P = 0.23$). Also associated with HED were prematurity, i.e., lower gestational age (P 0.0001), and such correlates of low gestational age as low birth-weight ($P = 0.002$), shorter Stage 1 labor ($P = 0.0005$), interval between membrane rupture and delivery ($P = 0.0005$), lower Apgar scores at 1 min ($P = < 0.0001$) and at 5 min (8.7 compared to 8.9, P .0001), premature labor ($P = 0.004$), admission of the child to the special care nursery ($P = 0.005$), and reduced likelihood of pitocin augmentation of labor ($P = 0.009$). The increased risk of HED among children who were small for gestational age did not reach nominal significance ($P = 0.09$). Children born in winter months were not at greater risk of HED than those born the remainder of the year ($P = 0.81$).

A total of 63 characteristics and experiences were included in the questionnaire sent to parents when the child was 6 years old. Only three qualitative variables had a distribution among children with HED that differed significantly from the distribution among children without these defects. Children with the HED were more likely than their peers to be left-handed ($P = 0.01$) and to have had a clinically evident measles infection ($P = 0.00008$). These children were less likely, however, than others to have received a screening evaluation for undue lead burden during early childhood ($P = 0.03$).

The cumulative distribution of umbilical cord blood lead levels is essentially the same among children whose teeth demonstrated HED as among children who did not (Fig 1, next page). Similarly, children who had HED had very much the same distribution of central dentin lead as did their peers who were without HED (Fig 2, next page).

Discussion

With approximately 200 comparisons, our finding that a handful achieved nominal statistical significance raises the possibility that some reflect random phenomena. Caution is advised in drawing inferences about our findings, especially those that reflect hypotheses not generated in previous studies.

Many of the antecedents and correlates of HED of the primary incisors identified in this study, as well as those reported in the literature (Table 1), are covariates of low socioeconomic status; e.g., prematurity / low birth-weight, maternal history of smoking, higher prepregnancy weight, delay in obtaining prenatal care,

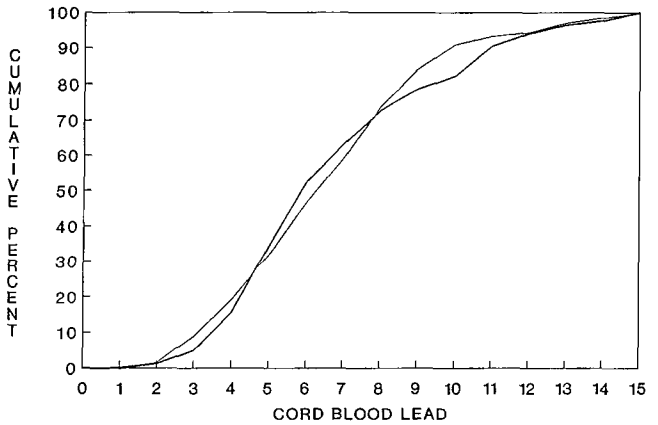

Fig 1. The cumulative frequency of umbilical cord blood lead levels (mcg/dL) of children whose primary incisors had a macroscopic enamel defect (heavy line) closely approximates that of children whose tooth lacked a defect (light line).

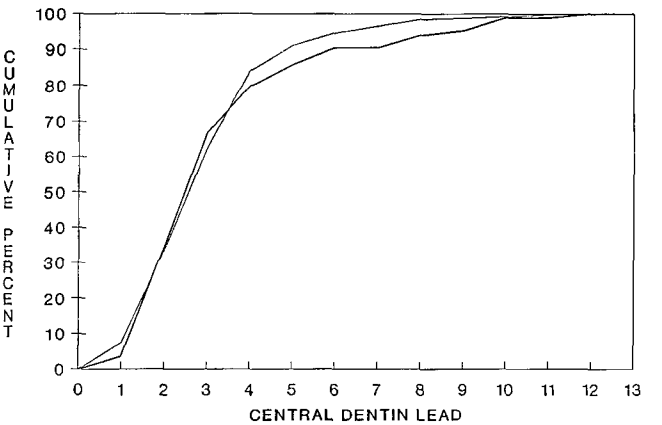

Fig 2. Primary incisors with a macroscopic enamel defect (heavy line) have a cumulative frequency distribution of central dentin lead (mcg/gm) very much like that of primary incisors without any such defect (light line).

lower rates of vaccine immunization, and failure to obtain lead screenings. Although most of the families in this study were highly educated, sufficient variability of socioeconomic correlates was present to allow these to be identified as antecedents of HED. Low socioeconomic status of a family may put a fetus or newborn at risk for developing HED of the primary incisors.

It is well documented that both prematurity and low birth-weight are more prevalent in lower socioeconomic groups.[29–31] Our finding that 42.1% of premature infants and 40.9% of low birth-weight infants had HED, compared with 17.6% of full-term babies and 17.4% of newborns of normal weight, is consistent with prevalences reported in similar children (Table 2). Typically, between 30 and 50% of premature/low birth-weight infants demonstrate HED, while the prevalence of HED in full-term newborns ranges between 10 and 20%. HED also were associated with lower Apgar scores at 1 and 5 min, which also may reflect low gestational age.[32] Children who were admitted to a special care nursery were more likely to have teeth with HED — also not surprising — because these children are often premature, of low birth-weight, or if full-term, have sustained a significant systemic insult. Shortened labor and reduced need for labor augmentation were also associated with the risk of developing HED. These factors are associated with low birth-weight[33] and thus may not provide additional information beyond that provided by low birth-weight.

One of the more obvious links between HED and low socioeconomic state is nutrition. Nutritional factors have been linked repeatedly to HED development (Table 1). Mothers and children of low socioeconomic status may have nutritional histories or behaviors that increase the fetus' or neonate's risk of developing HED. Children from "underdeveloped" populations have an increased prevalence of HED, and usually have poorer pre-, peri-,

Table 4. The mean value for the characteristic listed on the left for those children whose tooth did or did not have a HED

	Hypoplastic Enamel Defects		
	Yes	*No*	*P value*
Prenatal			
Maternal hematocrit	37.4	37.8	.13
Maternal smoking (years)	5.3	4.0	.0008
Prepregnancy weight (kg)	59.6	57.3	< .0001
Prepregnancy weight gain (kg)	13.5	13.6	.34
Perinatal			
Apgar score			
1 minute	7.6	8.0	< .0001
5 minutes	8.7	8.9	< .0001
Birth weight (kg)	3.2	3.5	.002
Gestational age (wk)	39.2	39.9	< .0001
Membrane rupture (hr)	6.2	8.2	.0005
Stage 1 labor (hr)	9.0	9.6	.002
Postnatal			
Number of ear infections	6.2	6.2	.69

and postnatal nutrition than those from "developed" populations.[8–17]

Neonatal hypocalcemia, often associated with HED development,[34–40] is a common finding in neonates and is more prevalent in those who are premature than in those born at term.[41–43] Some authors postulate that neonatal hypocalcemia is exacerbated by a low intake of human breast milk during the first week of life, which is common in preterm or low birth-weight infants.[36, 37, 44, 45] These low calcium levels may affect enamel formation, and thus, be responsible for HED.[46, 47]

Mellander et al.[48] and Noren[39] reported that infants born in winter months had higher prevalences of HED and theorized that lower exposure to sunlight in these months resulted in a concomitant decrease in the levels of vitamin D production and thus less calcium absorption. We did not find any higher risk for HED development among children born in winter months when compared with those born in the remainder of the year.

Maternal genital infections are not only most common in lower socioeconomic women, but these infections also appear to increase the likelihood of premature onset of labor and premature rupture of membranes,[49, 50] both of which were associated with HED in this study. These infections are associated with changes in the fetal environment, and thus may interfere with normal development.

Some of the HED antecedents with socioeconomic correlates may have more direct effects on enamel formation. For example, maternal smoking is associated with decreased birth-weight[51] which in our data was associated with an increased risk of HED. The offspring's risk for developing HED also increased if prenatal care began later than the first trimester. Maternal smoking and delayed prenatal care both are plausible biological reasons for increased risk of HED.[52–56] They also have sociodemographic correlates that might place a baby at increased risk for HED.[57]

Our finding that measles susceptibility is associated strongly with HED of the primary incisors may very well reflect inadequate childhood immunization, another correlate of socioeconomic status.[58, 59] This explanation is more plausible than a direct effect of the rubeola virus on the developing dentition, since a late postnatal measles infection cannot affect the perinatal development of the primary incisors.

We found that children who did not have their blood tested for elevated lead levels during infancy and early childhood were at increased risk for HED. Although lead screening might be expected to convey information about socioeconomic status of the family, we found no relationship between lead screening and maternal education, one of the best measures of socioeconomic status. Thus, it is unclear what information is conveyed by the lead screening variable.

The strong association between left-handedness and HED has not been reported previously . This association could reflect the sociodemographic correlates of left-handedness such as birth order where greater birth order, a socioeconomic correlate, is associated with increased likelihood of left-handedness.[60–62]

Previously unreported are our findings that increased prepregnancy maternal weight and Tylenol use were related significantly to the risk of HED development. Mothers from lower socioeconomic groups tend to have a higher body mass index[63] and are less likely to follow admonitions to avoid medications during pregnancy.[64]

Consumption of more than three cups of tea per day during the first trimester pregnancy was significantly related to the risk of HED development; however the same was not true for an equal consumption of coffee (Table 3). Although the amount of tea consumed later in pregnancy is not known, we assume that those who consumed tea during one trimester are most likely to have consumed tea during other trimesters. Because tea has an extremely high fluoride content,[65, 66] the excessive ingestion of a fluoride-rich substance during formation of the enamel of the primary incisors may predispose these teeth to developmental enamel defects.[67] The fluoride may increase the risk of developing HED via a direct toxic effect on the ameloblasts, or may act by decreasing the serum calcium level.[46]

Although previous studies have demonstrated a positive relationship between hearing impairments and HED of the primary incisors,[68, 69] our data failed to confirm this association. It should be noted that in our study, hearing impairment was based solely on parental history, and thus may be a less sensitive criterion than that used by other investigators.

The risk of HED did not increase with increasing umbilical blood lead content (Fig 1). Pearl and Roland[70] reported delayed eruption of the primary dentition in a child exposed to high prenatal lead levels. Our failure to demonstrate any lead/HED relationship may reflect the low lead levels in our sample. No study to date, however, has demonstrated a relationship between prenatal lead exposure and HED of the primary teeth.

Although pitting hypoplasia of permanent teeth has been associated with postnatal lead exposure,[71] we did not find any relationship between postnatal lead exposure as measured in dentin lead levels of the returned exfoliated primary incisors and HED of these teeth (Fig 2). The dentin lead levels of children in our samples are also much lower than those measured in children who have documented lead poisoning.[72]

Some of our findings were not anticipated, while others fit into previously stated hypotheses. We advise caution in drawing inferences about these results. Additional investigation is needed to delineate more pre-

cisely the associations between specific pre- and perinatal nutritional and infectious factors, socioeconomic status, and the development of HED.

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