Community Dent Oral Epidemiol 2008; 36: 179–189

COMMUNITY DENTISTRY AND ORAL EPIDEMIOLOGY

Effect of early childhood malnutrition on tooth eruption in Haitian adolescents

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Psoter W, Gebrian B, Prophete S, Reid B, Katz R. Effect of early childhood malnutrition on tooth eruption in Haitian adolescents. Community Dent Oral Epidemiol 2008; 36: 179–183. © 2007 The Authors. Journal compilation © 2007 Blackwell Munksgaard

Abstract – *Objective:* The objective of this retrospective cohort study was to determine the effects of early childhood protein-energy malnutrition (EC-PEM) and current nutritional status as defined by anthropomorphic measures on the exfoliation and eruption patterns of teeth among adolescents. *Methods:* Oral clinical examinations were conducted in 2005 using World Health Organization (WHO) diagnostic criteria on 498 11- to 13-year-old Haitians for whom early childhood malnutrition data were available. Anthropomorphic records (weight-for-age) from the Haitian Health Foundation computerized database on children from birth through 5-years old were utilized. Current heights and weights were ascertained. Both sets of data were converted to *z*-scores based on the National Center for Health Statistics (NCHS) referent database. Based upon these *z*-scores, EC-PEM and current malnutrition categories were developed for this study. The analyses separately regressed the number of primary and permanent teeth on age, gender, EC-PEM status and current nutritional status. *Results:* Both a delayed exfoliation of primary teeth and a delayed eruption of permanent teeth were associated with EC-PEM and current stunting in adolescence. The observed associations were either direct and statistically significant or indirectly demonstrated by presenting evidence of confounding. The overall interpretation of the models is that malnutrition beginning in the earliest years and extending throughout childhood influences the exfoliation and eruption of teeth. *Conclusion:* These findings present evidence of an association between tooth exfoliation/eruption patterns and both EC-PEM and nutritional insufficiency (stunting) throughout childhood. This observed delay in the exfoliation of the primary dentition and in the eruption of the permanent dentition has practical significance in interpreting age-specific dental caries data from populations with different malnutrition experiences.

Key words: eruption; exfoliation; malnutrition; permanent teeth; protein-energy malnutrition

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Submitted 23 June 2006;
accepted 28 November 2006

Early Childhood Protein-Energy Malnutrition (EC-PEM) is implicated in over half of the thirteen million worldwide deaths of children aged 5 years and younger (1). While typically viewed as a problem associated with the developing world, EC-PEM occurs globally including even the disadvantaged populations within the 'developed, industrialized' countries (2, 3). EC-PEM is actually a spectrum of relative energy and protein deficiency, generally taking place concurrently. The relationship between EC-PEM and acute infections is a complex one as EC-PEM adversely affects the immune system leading to an increased risk of infection, while acute diseases may cause nutritional imbalances leading to EC-PEM. The appreciation of this complex relationship has led to the contemporary view of EC-PEM being a syndrome, which includes energy, protein and micronutrient intake deficiencies as well as frequent infectious disease episodes (4).

One growth and development manifestation of the effects of EC-PEM is an alteration in tooth

doi: 10.1111/j.1600-0528.2007.00386.x

eruption timing. A recent literature review on the relationship of EC-PEM with the eruption of the primary dentition reports a rich body of evidence that EC-PEM is consistently associated with delayed eruption of the primary dentition. However, reports of the effect of EC-PEM on eruption timing of the permanent dentition are extremely rare (5). The only published longitudinal studies of the effect of EC-PEM on the eruption of the permanent dentition have presented a limited and conflicting view of this relationship (6, 7). One reports a delay associated with malnutrition, but proposes that this delay was related to treatment changes prolonging primary tooth retention. The other study, reporting an advance in the eruption of some permanent teeth in malnourished children. Therefore, the answer to the question 'how does malnutrition in childhood effect permanent tooth eruption?' remains unknown and is the subject of the study reported here.

There are four specific circumstances surrounding the unfolding of a natural epidemiologic experiment that are pertinent to this study. First, the past and present economic and health realities of life in rural Haiti results in a high prevalence of malnourished children (40–75% in many areas, depending on the definition used) (8). Second, despite the best efforts of the Haitian Health Foundation (HHF) Primary Care Outreach Program in the Jeremie region of Haiti, 22% of the children are chronically malnourished during early childhood. Third, the HHF Primary Care Outreach Program has maintained a weight and age database since 1988. Lastly, the HHF has established and continues to operate a network. This network can recruit highly accessible subjects into a study via its active community health programmes currently involving over 200 000 individuals in the Jeremie region. As a result of these four specific circumstances, a large database of children with accurate weight-for-age anthropomorphic assessment of their malnutrition exposure for the first 5 years of life exists.

The purpose of this retrospective cohort study was to determine the effects of EC-PEM and current nutritional status as defined by anthropomorphic measurements on the exfoliation timing of the primary and eruption timing of the permanent dentition. The database for this study is the serial weight-for-age data collected between 1988 and 1996, and clinical examination and questionnaire data collected in 2005 in a population of 11–13 years olds who had been continuously living in a remote area of rural Haiti.

Methods

Overview

This paper reports on a retrospective cohort study of the effect of EC-PEM and adolescent nutritional status on the exfoliation of the primary teeth and the eruption of the teeth of the full permanent dentition, excluding third molars. Records (weight for age) from the HHF computerized database on children from birth through 5-years old were utilized. These data were converted to *z*-scores based on the National Center for Health Statistics (NCHS) 1978 data used as a Centers of Disease Control and Prevention (CDC) (9) and World Health Organization (WHO) reference database (10–12). Based upon these *z*-scores five malnutrition levels of early childhood nutritional sufficiency were created for this study. Additionally, using height and weight data collected during examinations in 2005, current anthropomorphically defined nutritional status categories were established for normal, stunting, wasting, and the combination of stunting and wasting. Oral clinical examinations on 510 children, ages 11–13 years old were conducted in 2005 using WHO diagnostic criteria (13). The analyses separately regressed the number of permanent and number of primary teeth on age, gender and early childhood malnutrition status, as well as current anthropomorphic nutritional classifications. This study was approved by the New York University Medical School Institutional Review Board.

Study sample

The 1988–1996 HHF database consists of 15 482 individual subject records. Death ($n = 541$) during the 1988–1996 period and enrolment into the HHF system for less than 3 years (see exposure definition below) left 9403 potential subjects for this study (Fig. 1). Of these potential subjects, 53% ($n = 4990$) met the required minimum of two recorded weights per year for at least three of the first 5 years of life. As several villages were no longer part of the HHF system, 918 potential subjects from these villages were excluded leaving 4072 eligible subjects. Because of the difficulty in travelling in rural Haiti, the current study's sampling frame was then designed to include all road accessible villages ($n = 1767$ subjects, 13 villages) and those nonroad assessable villages that provided the greatest yield of subjects ($n = 1396$ subjects, 6 villages). Thus 76% of the eligible

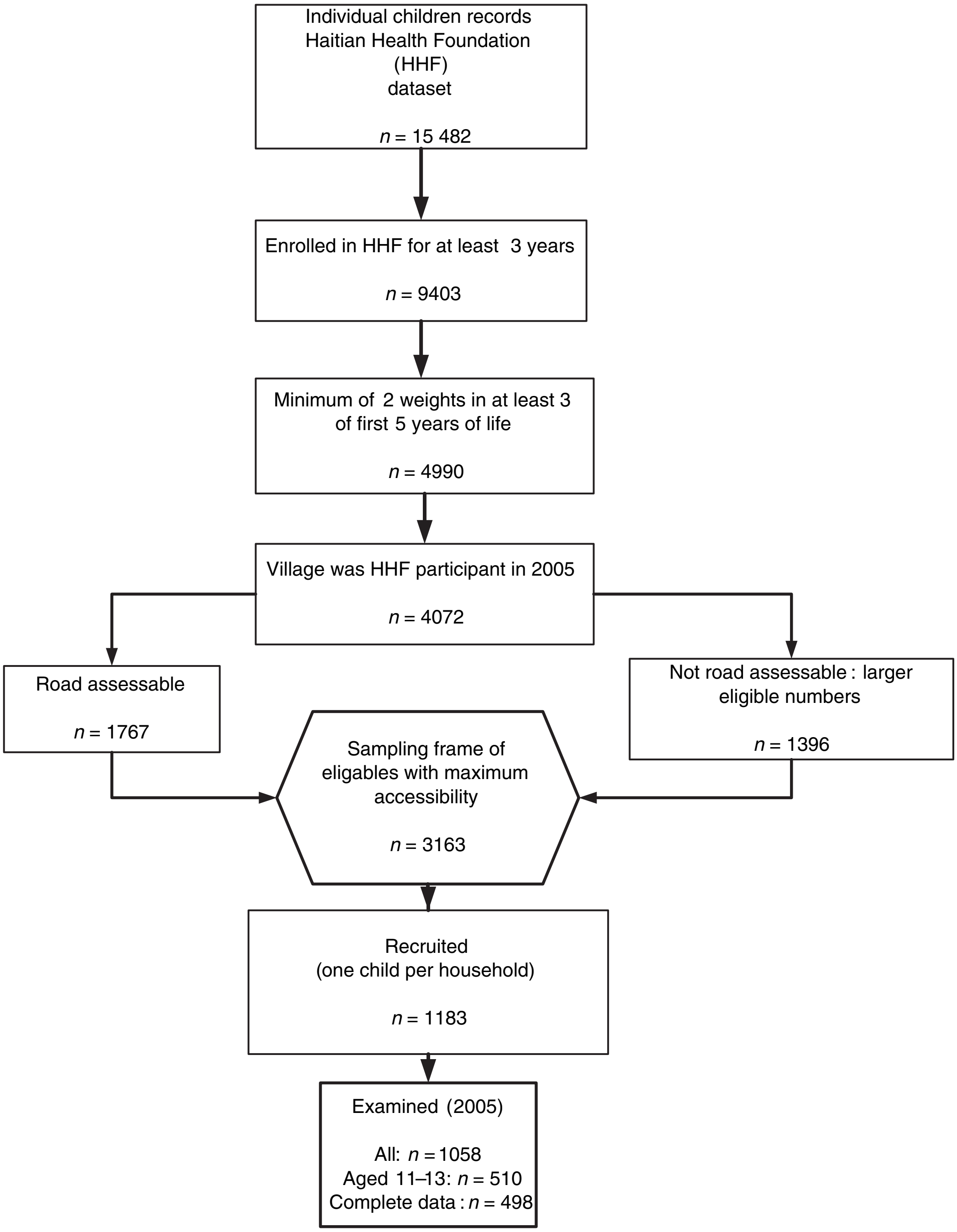

Fig. 1. Sample selection flow chart.

children (n = 3163) were included in the sampling frame to assure a recruitment of one child per household and a target of over 1000 subjects aged 11–19 years in 2005.

Two recruiters visited each study village between November 2004 and April 2005. Mothers of eligible children who were invited to participate gave a verbal consent to an informed consent read to them in Creole. Of the 3163 children comprising the sampling frame, 31 had died since 1996 and 10 mothers refused (0.3%) to participate. Recruitment was limited to include only one child per household, the oldest available child being enrolled in the study. A total of 1183 eligible 11–19 year olds were enrolled in the parent study. Within this total sample of 1183 11–19 year olds, this report is based on the 498 subjects who were aged 11–13 years at the time of the field examination in the summer of 2005, and had complete data. This criterion of only including 11–13 year olds, i.e. less than 14 years old, in this analysis was employed to capture the traditionally-established eruption period for the permanent canines, first and second premolars, and second molars.

Exposure definition

The first step in the identification of subjects for this study was the development of exposure definitions for each of the five EC-PEM groups. The basis of definitions for the primary analyses is derived from weights of the subjects during their first 5 years of life for the 1988–1996 period. The scales used to weigh the children during their first 5 years of life were UNICEF issued and calibrated at the beginning and during the process of obtaining weights. These data were recorded on individuals' HHF health cards by village resident HHF health agents. These agents also recorded date of births which were subsequently used to produce age at examination. Data was entered in an on-going manner into the HHF computerized data system. These data have been used by the CDC in a case control study (14), and the data assessed in a 10-year programme evaluation study for the United States Agency for International Development (USAID) that commended the low error rate (5%) for a field-based programme (15).

The early childhood exposure definitions are based upon EC-PEM magnitude and frequency. Each eligible age-year (at least two weights in an age-year), birth through 5 years old was classified by weight-for-age as severe (z-scores ≤ -2), questionable (z-scores > -2 and ≤ -1), and normal (z-scores > -1). This severity score combined with the frequency of the severity score were used to produce five hierarchal EC-PEM exposure categories (Table 1). All EC-PEM definitions used a z-score based upon the weight-for-age for each child on a given visit, normalized with NCHS data (10–12). A z-score of 0.00 indicates a weight-for-age equal to the median for a child of the same gender in the NCHS database. A z-score less than 0.00 indicates a weight-for-age that is the indicated number of standard deviations below the median for a child of the same gender and age in the NCHS database. The NCHS database was selected for normalization to allow international comparisons as recommended by the WHO. Height-for-age (HAz) data were not available because of cultural concerns; measuring an infant's height is associated with measuring for a coffin size.

Weight and height measurements taken during the 2005 field examinations were likewise categorized based on anthropomorphic measures to be used in multivariable models to assess any effect by continued chronic and more recent acute malnutrition. Age and gender standardized z-scores, again based on the NCHS database were computed for HAz and body mass index-for-age scores (BMIz). These were then used to classify the subjects as: stunted (HAz ≤ -2), wasted (BMIz ≤ -2), and stunted and wasted (HAz and BMIz ≤ -2) (Table 1). Subjects were classified exclusively to one category only, and for this age group BMIz rather than height-for- weight is used to determine wasting (9, 12).

During the field operations phase data were obtained on other variables that were considered as potential confounding variables. An interviewer-administered, structured-questionnaire to assess socioeconomic and demographic information was administered to the mother/guardian of the child. Interviewers received 3 days of training by experienced senior researchers in a standardized administration of the questionnaire. Staff were trained and calibrated in the height and weight measurements using a standard Detecto Balance Beam Scale; the study scales themselves were re-calibrated

Table 1. Early childhood and adolescent malnutrition categories

Period	Exposure	Definition
Birth-5 years	Regular malnutrition	[a]z-scores ≤ -2.0 in at least 3 years in the first 5 years of life
	Intermittent malnutrition	[a]z-scores ≤ -2.0 in 1 or 2 years in the first 5 years of life
	Regular questionable malnutrition	[a]z-scores ≤ -1.0 in at least 3 years in the first 5 years of life
	Intermittent questionable malnutrition	[a]z-scores ≤ -1.0 in 1 or 2 years in the first 5 years of life
	No malnutrition	[a]All z-scores greater than –1
Adolescence (2005)	Stunted	Height-for-age ≤ -2 z-score
	Wasted	Body mass index for age ≤ -2 z-score
	Stunted and wasted	Height-for-age ≤ -2 z-score and Body mass index for age ≤ -2 z-score
	Normal	Height-for-age and Body mass index for age z-scores > -2

[a]Weight-for-age.

daily on arrival in a study village, as a routine part of the field operations.

Outcome measurements

Four dentists were trained and calibrated to WHO standards for dental caries examinations by a WHO-criteria trained calibrator. These four dentists performed all oral examinations. Preceding the beginning of the field examinations the examiners were calibrated to at least 90% agreement and a Kappa score of at least 0.75 to the referent examiner for decay, missing (because of caries), and filled tooth surfaces (DMFS and dmfs) utilizing WHO diagnostic criteria (13). Tooth eruption was defined as having occurred if any tooth surface had pierced the alveolar mucosa.

Field operations

Field data collection was conducted in the subjects' villages of residence between May and August, 2005. Field examinations were conducted under normal daylight conditions supplemented by portable headlamps and using mirrors and #23 explorers. The data collected relied solely on the visual-tactile examination performed by the trained examiners without the use of dental radiographs. All data were recorded on carbonless-copy data entry forms. To assess intra- and inter-examiner reliability, each examiner performed duplicate examinations on 20% of the sample of subjects examined. The field supervisor arranged the re-examination in such a way that the examiners were blinded as to which children would be re-examined.

Data management

All data were double entered into an EpiInfo 2000 database and confirmed against the original datasheets. These data were then converted to a SPSS dataset. The data were then cleaned using frequency counts and graphing.

Statistical analysis

Descriptive statistics were produced. The unit of analysis was the individual. The number of primary teeth and the number of permanent teeth, as an individual's aggregate score were separately regressed on age (months), gender, EC-PEM status and current (2005) anthropomorphic classifications of stunting, wasting, and stunting and wasting. Two-sided P-values ≤ 0.05 were considered statistically significant.

Results

Descriptive statistics for the 498 children at the time of clinical exams are presented in Table 2. The mean age of the subjects was 12.46 years, or 149.5 months old (SD = 7.3). Although age differences between the malnutrition groups were statistically significant, the maximum mean difference was 3.3 months. Current height-, weight- and BMI-for-age z-score values from the 2005 examinations demonstrated a statistically significant relationship across the malnutrition groups with all current average anthropomorphic measures decreasing with increasing severity levels of EC-PEM. Although more males than females were sampled the gender differences between the EC-PEM groups was not statistically significant. In terms of the average numbers of primary and permanent teeth, the age-adjusted regression P-values were statistically significant between malnutrition categories; however, a nonlinear trend was suggested and a dichotomization combining the first three categories against the two most severe categories (any versus no z-score ≤ -2 in the first 5 years of life) was made. Intra- and inter-examiner DMFS Kappa scores were 0.84 and 0.63, respectively.

The unit of analysis was the individual using either the subjects' total number of primary or permanent teeth as the outcome variable regressed on EC-PEM categories, age, gender and current (2005) adolescent anthropomorphic categories indicative of stunting, wasting and stunting and wasting. The initial regression model treating the EC-PEM categories as dummy variables supported a threshold effect among children having any frank malnutrition episode, i.e. any z-score ≤ -2 in early childhood. Regression analyses were then repeated as described above with EC-PEM as a dichotomized variable, malnutrition or no malnutrition (all early childhood z-scores > -2).

The regression results for the number of primary teeth representing exfoliation timing are presented in Table 3. In the full model including all covariates, the EC-PEM group demonstrated a statistically significant (0.049) finding of 0.49 more predicted primary teeth. The most parsimonious model, dropping covariates with a P-value less than 0.1 in a stepwise regression procedure resulted in a predicted value of 0.65 additional teeth in the malnourished group (P = 0.006). However, the magnitude of change in the coefficient, i.e. an

Table 2. Descriptive statistics of early childhood protein-energy malnutrition (EC-PEM) among 500 Haitian children ages 11 through 13 years old in 2005

	No malnutrition	Questionable intermittent malnutrition	Questionable regular malnutrition	Regular intermittent malnutrition	Regular malnutrition	Total	*P*-value	Correlation
n	91	123	48	150	86	498		
Age (months) (SD)	148.9 (7.2)	148.6 (7.4)	151.9 (5.7)	148.8 (7.2)	151.6 (7.6)	149.5 (7.3)	0.03[a]	
z-scores (2005)								
Height-age *z* (mean) (SD)	−1.4 (1.1)	−1.9 (0.95)	−2.0 (1.2)	−2.6 (1.1)	−3.0 (1.0)	−2.2 (1.2)	<0.001[a]	0.481[c]
Weight-age *z* (mean) (SD)	−1.1 (0.7)	−1.6 (0.6)	−1.8 (0.6)	−2.0 (0.6)	−2.3 (0.6)	−1.8 (0.7)	<0.001[a]	0.551[c]
Body mass index *z* (mean) (SD)	−0.58 (0.7)	−0.98 (0.8)	−1.3 (1.2)	−1.4 (0.9)	−1.6 (0.9)	−1.2 (0.9)	<0.001[a]	0.396[c]
Gender (*n*, %)								
Female (%)	44 (48.4)	61 (49.6)	18 (37.5)	70 (46.7)	34 (39.5)	227 (45.6)	0.453[b]	
Male (%)	47 (51.6)	62 (50.4)	30 (62.5)	80 (53.3)	52 (60.5)	271 (54.4)		
Number of permanent teeth	24.83 (4.13)	24.96 (3.79)	25.31 (3.67)	24.12 (4.59)	24.23 (4.66)	24.59 (4.25)	0.016[d]	
Number of primary teeth	1.37 (2.66)	1.2 (2.31)	1.1 (2.48)	1.87 (3.02)	1.77 (3.01)	1.52 (2.75)	0.011[d]	

[a]ANOVA.
[b]Chi-square test (2 sided).
[c]Spearman Rank correlation coefficient, $P < 0.01$.
[d]Regression adjusted for age.

increase of 22%, or 0.14 predicted teeth, suggested a confounding effect, which was associated with stunting rather than wasting. A new model that included an 'any stunting' variable, i.e. any HAz *z*-score ≤−2 was incorporated into the model. This result demonstrated a statistically significant increase in the number of primary teeth in the malnourished in early childhood group (0.51) and a nonstatistically significant increase in primary teeth in stunted subjects (0.39). The addition of the 'any stunting' variable resulted in a 27% change in the EC-PEM regression coefficient suggesting a confounding effect. An interaction term between EC-PEM and 'any stunting' was not statistically significant.

An inverse pattern was observed in the number of permanent teeth with EC-PEM as shown in Table 4. The fully adjusted model found the EC-PEM group having a predicted 0.55 fewer teeth than the children without EC-PEM, although not statistically significant. Stunted children had a statistically significant ($P = 0.028$) 0.89 fewer teeth, while stunted and wasted subjects approached statistical significance ($P = 0.58$) with a predicted average of 1.28 fewer teeth than normal subjects. Interestingly, the most parsimonious model derived from a stepwise procedure, resulted in a predicted 0.9 fewer teeth for the malnourished group ($P = 0.009$). However, unlike the primary teeth model, when the currently 'any stunted' variable was included in the model, this variable was statistically significant (0.96 fewer permanent teeth) and the EC-PEM group, while having a predicted value of 0.58 fewer teeth, did not achieve statistical significance ($P = 0.117$). The regression coefficient, for any stunting, had a 20% change (from -0.96 to -01.16) when the EC-PEM variable was dropped from the model, suggesting an EC-PEM confounding effect. An interaction term between EC-PEM and 'any stunting' was not statistically significant.

All models consistently showed a greater delay in boys compared with girls when adjusted for age, EC-PEM status and current anthropomorphic classification. When regression models were limited to the permanent canines, premolars and second molars, similar findings were observed thereby indicating robust estimates of effect. Lastly, analyses using regression models in which the outcome variables, primary decayed, missing because of caries, and filled surfaces dmfs, dmft, and dmfs divided by the number of primary surfaces of each subject (dmfs/number) revealed no statistically

Table 3. Results of regression models to predict primary tooth exfoliation in Haitian children from nutritional status

Model	Variables	Regression coefficient	SE	*t*	*P*-value
Full model	Intercept	15.40	(2.40)		
	Age (months)	−0.11	(0.02)	−6.59	<0.009
	Gender[a]	0.97	(0.23)	4.18	<0.009
	EC-PEM[b]	0.49	(0.25)	1.96	0.051
	Stunting (2005)[c]	0.32	(0.27)	1.17	0.244
	Wasting (2005)[d]	−0.26	(0.52)	−0.50	0.616
	Stunting and Wasting (2005)[e]	0.59	(0.45)	1.31	0.191
	Adjusted r-square = 0.114				
Parsimonious model	Intercept	15.16	(2.40)		
	Age (months)	−0.10	(0.02)	−6.51	<0.009
	Gender[a]	0.99	(0.23)	4.26	<0.009
	EC-PEM[b]	0.65	(0.23)	2.79	0.006
	Adjusted *r*-square = 0.114				
Final model	Intercept	15.44	(2.40)		
	Age (months)	−0.11	(0.02)	−6.66	<0.009
	Gender[a]	0.98	(0.23)	4.22	<0.009
	EC-PEM[b]	0.51	(0.25)	2.08	0.039
	Any stunting[f]	0.39	(0.25)	1.55	0.123
	Adjusted r-square = 0.117				

[a]Referent category = female.
[b]As dichotomous variable: referent category = no malnutrition (all of first 5 years of life with a *z*-score > −2).
[c]Height-for-age *z*-score ≤−2 (2005).
[d]Body mass index -for-age *z*-score ≤−2 (2005).
[e]Height-for-age and body mass index for age *z*-scores >−2.
[f]Referent category = no stunting.

Table 4. Results of regression models to predict permanent tooth eruption in Haitian children from nutritional status

Model	Variables	Regression coefficient	SE	*t*	*P*-value
Full model	Intercept	−0.21	(3.61)		
	Age (months)	0.19	(0.02)	7.90	<0.009
	Gender[a]	−1.93	(0.35)	−5.53	<0.009
	EC-PEM[b]	−0.55	(0.38)	−1.45	0.149
	Stunting (2005)[c]	−0.89	(0.41)	−2.02	0.028
	Wasting (2005)[d]	0.08	(0.78)	0.106	0.916
	Stunting and Wasting (2005)[e]	−1.28	(0.67)	−1.90	0.058
	Adjusted *r*-square = 0.164				
Parsimonious model	Intercept	0.46	(3.62)		
	Age (months)	0.19	(0.02)	7.71	<0.009
	Gender[a]	−1.96	(0.35)	−5.61	<0.009
	EC-PEM[b]	−0.91	(0.35)	−2.61	0.009
	Adjusted *r*-square = 0.158				
Final model	Intercept	0.24	(3.61)		
	Age (months)	0.19	(0.02)	7.99	<0.009
	Gender[a]	−1.94	(0.35)	−5.57	<0.009
	EC-PEM[b]	−0.58	(0.37)	−1.57	0.117
	Any stunting[f]	−0.96	(0.38)	−2.53	0.012
	Adjusted *r*-square = 0.167				

[a]Referent category = female.
[b]As dichotomous variable: referent category = no malnutrition (all of first 5 years of life with a *z*-score > −2).
[c]Height-for-age *z*-score ≤−2 (2005).
[d]Body mass index -for-age *z*-score ≤−2 (2005).
[e]Height-for-age and body mass index for age *z*-scores > −2.
[f]Referent category = no stunting.

significant findings by EC-PEM or current nutritional status. No primary tooth restorations were observed. Thus, any differential in numbers of teeth erupted between the EC-PEM groups cannot be explained by a differential primary teeth caries experience.

Discussion

While EC-PEM has been demonstrated to be associated with the delayed eruption of primary teeth (5), limited findings have been reported regarding eruption of the permanent dentition. Investigations of the effect of EC-PEM on the full permanent dentition are challenging in that they require serial records of anthropomorphic measurements in the infant and toddler years and the ability to follow-up those children after a time-lag of eight or more years. The HHF program's 1988–1996 database from rural Haiti presented a unique opportunity to study this relationship.

The anthropomorphic assessment of malnutrition is the historical gold standard for this exposure in children (10). The NCHS/CDC anthropometry reference database is used to compute subject *z*-scores and develop the WHO recommended growth curves for international use (10–12). *z*-scores are also referred to as SD units from the median of the NCHS reference population for the same age and gender (9); a *z*-score of <-2 is considered as a low anthropometry measurement. Four different ratios are commonly used each denoting a different aspect of malnutrition (9). The ratio HAz measures stunting or chronic past malnutrition. The ratios weight-for-height or BMIz measure wasting, which indicates current malnutrition; weight-for-height can be computed to age 11.5, BMIz is used after that age. The ratio weight-for-age is a composite of weight and height for an age and is useful at younger ages and with serial weightings.

In a review of the literature, Alvarez and Navia state that while tooth eruption timing is multifactorial (16), the strongest relationship has been between eruption and skeletal growth. Several studies using height and/or weights found correlations with tooth eruption (6, 7, 17–19). The data from this sample likewise found correlations ($P \leq 0.01$) between HAz and weight-for-age of 0.195 and 0.153, respectively. As tooth eruption involves both maturation of the tooth and the ability of the overlying bone to reform allowing tooth eruption, factors that negatively affect these processes may delay eruption. Some brief notes will orientate the reader and direct those interested in this area of basic research outside the scope of this paper.

Long bone growth occurs at the bone growth plate through endochondrial ossification. This process is regulated by local and systemic hormones including PTH, and elements of the growth hormone insulin-like growth factor 1 axis, which can be influenced under fasting conditions (20). Parathyroid hormone-related protein (PTHrP) mediates osteoclasts activity in the dental follicle 'in a manner analogous to the osteoblast-mediated process in the peripheral skeleton' (21). Importantly in interpreting the findings reported here is a review that found a 'metabolic shift' in children malnourished in the first year of life, independent of birth weight, i.e. intra-uterine nutritional deprivation. Specifically, malnutrition preprogrammed insulin sensitivity, glucose tolerance and lipid profiles in early adulthood (22). Such early childhood preprogramming could be a mechanism applied to other endocrine and molecular systems that affects later growth and development.

The two previous reports on EC-PEM and permanent tooth eruption each had some limitations and were contradictory. One study used time-series data, over the World War II and post World War II period and drew its conclusions upon ecologically based nutritional assumptions on children between the ages of 7 and 13 years and school dental records (6). The author of this study, which reported a delay in the loss of primary teeth in children up to the age of 13 years associated with war-time nutritional insufficiencies hypothesized that a similar 'delay' in the eruption of permanent teeth was because of decreased war-time primary teeth caries (as a result of decreased sugar availability and consumption), which, in turn, led to an increase in conservative dental treatment, i.e. fewer extractions of primary teeth as compared with prewar primary tooth extraction demands. Thus, war-time conditions favouring prolonged primary tooth retention was suggested to be the result of this alteration in treatment modality and the author concluded that no true difference in eruption patterns primarily because of nutritional stress was likely. Rather, the author postulated that the observed postwar permanent tooth eruption 'delay' was, in fact, the 'normal' age for eruption; the delay being in fact relative to the earlier study period in which primary tooth extraction induced 'early' eruption of the permanent teeth (6). However, despite the authors' preference for their 'nonnutrition stress' explanation of findings, that study did note a very slight (albeit not statistically significant) delay in the eruption of the first permanent molars and a statistically significant delay in the eruption timing of second permanent molars, neither of which have antecedent primary teeth.

In the only other longitudinal study of EC-PEM and the permanent dentition, Alvarez reported, to his group's surprise, early eruption of the permanent first molars and permanent incisors among Peruvian children having EC-PEM (7). This caries study of the primary and permanent teeth included 94 six-year-old children who were a subset of 209 children followed from 6 to 11 months of age when they were classified as normal, stunted, wasted, or stunted and wasted. The children previously classified as stunted and wasted had statistically significant more permanent teeth (incisors and first molars). However, this very brief report did not note the nutritional status at the time of the 6-year examinations, and no additional information was reported. Thus, unlike the effect of EC-PEM on primary dentition eruption for which numerous studies have found a delayed eruption in nutritionally stressed children, these two previous studies comprise the published literature on the effect of malnutrition on the eruption of permanent teeth with the study reported here adding to this limited body of literature.

This study identified a delayed exfoliation of the primary teeth confirming previous reports of an association with EC-PEM by extending this finding to the later exfoliating primary teeth. However, the confounding effect observed with current stunting included in the analytic model raises some caution in the interpretation of this result. Although no effect was found for currently wasted, i.e. recently experiencing severe malnutrition, the stunted in 2005 children were likely chronically malnourished beyond the age of 5 years old and could continue to be experiencing nutritional stress. Absent growth data for the period between 1996 and the examinations in 2005, we cannot exclude this possibility. Alternatively, this population may have been preprogrammed by EC-PEM for stunting, i.e. unable to experience a timely growth catch-up, or the teeth, through various molecular mechanisms, may have been preprogrammed for a delayed exfoliation secondary to a delayed development or eruption of their replacement permanent teeth. A most conservative interpretation of the findings reported here is that chronic malnutrition through childhood that begins in the early childhood period delays primary teeth exfoliation into early adolescence. This is consistent with the limited literature reporting on exfoliation and malnutrition (6, 7, 17).

Findings from this study regarding the eruption timing of the permanent teeth suggest that chronic malnutrition extending beyond the early childhood is correlated with delayed eruption; but as with primary teeth exfoliation there is also an EC-PEM effect that may be either a direct contribution to the delayed eruption or EC-PEM may be a predictor of continuing nutritional stress. The Spearman correlation coefficient for EC-PEM and HAz in 2005 is a statistically significant 0.48.

The findings reported here modify rather than directly contradict Alvarez's (1995) report of an accelerated eruption in the permanent dentition. Alvarez reported on only 94 children then 6 years old; the analysis was thus limited to permanent incisors and first molars. As those permanent teeth in this current study were all fully erupted at the time of the examinations of this investigation, we cannot comment on the eruption timing of these teeth, only that at ages 11 through 13 years old, there is a delay in permanent tooth eruption of the *complete* permanent dentition as defined by the number of teeth. The findings reported here reflect the findings reported by Toverud's analysis of a population of Norwegian children, although his interpretation of that data led him to a different conclusion than this study (6).

A clear gender difference was found, adolescent boys' permanent teeth eruption being delayed relative to adolescent girls. This could be associated with gender differences in pubertal growth rates between genders with females experiencing earlier puberty. This study did not have measures assessing maturation levels or contemporary serial anthropomorphic measures to examine growth trajectory.

Strengths of this study include the cohort study design, a large sample size, longitudinal data, trained and calibrated examiners, and the robustness of the results across the several models. Further, when analyses were limited to canines, premolars and second molars, essentially identical results were obtained. There are several limitations. The early childhood weights were collected by a standardized procedure designed for clinical rather than scientific purposes. This and possible data entry errors of that data may have introduced some misclassification; however, any such misclassification would be random and result in a tendency toward the null in the analyses. There are no anthropomorphic measures between 1996 and 2005, resulting in our inability to precisely define a critical biological point of malnutrition effect.

However, as we discuss above, these data do support malnutrition prior to early adolescence being associated with a delay in permanent tooth eruption. The lower limit of the sample age range somewhat limited the analyses to small differences in the tooth numbers, e.g. a sample comprised of children 9 or 10 years old would have included a greater number of actively erupting teeth and would have allowed alternative analytic approaches, e.g. well powered analyses at the individual tooth level. Lastly, no information regarding other developmental measures was ascertained. This coupled with the sample age range precludes these data from being utilized to incorporate teeth numbers into a developmental, rather than age, developmental milestones index.

These findings present evidence of an association between childhood severe chronic malnutrition and delayed exfoliation of the primary teeth as well as delayed eruption timing for permanent teeth. That this late effect is related to chronic rather than acute severe nutritional insufficiency is evident from the inconsequential effect of current wasting. Whether the biological consequences of malnutrition are directly initiated with EC-PEM or with continuing nutritional stress in the pre-adolescent years cannot be determined from these data. Although, if adolescent stunting is significantly associated with EC-PEM, i.e. little or no growth catch-up, then these data could be interpreted as an early childhood malnutrition episode related delay in exfoliation and eruption. This would suggest a preprogramming of some element(s) of the molecular-level aspects of tooth exfoliation/eruption. Importantly, the findings do suggest a severe malnutrition effect on exfoliation/eruption that is consistent with Toverud's earlier report and with most reports regarding primary teeth eruption. Although this study cannot directly contradict Alverez's report of an earlier eruption of permanent incisors and first molars, that study's $n = 94$ may have been small enough to produce a spurious finding.

Given this is the first comprehensive study with longitudinal data on a cohort of subjects, future studies on the relationship of malnutrition and tooth eruption/exfoliation patterns should be conducted to confirm or refute the conclusions drawn here. Ideally, there is a need for continuous nutritional measurements throughout the pre-adolescent period. However, as extensively described for the primary teeth by Alvarez and Navia, these findings have practical significance in interpreting age-specific dental caries data from populations with different malnutrition experiences because of the differential tooth exposure time to cariogenic risk factors in these populations. The delayed exfoliation of the primary teeth in malnourished children should increase the age-specific dmfs in older children and the delayed eruption of the permanent teeth should lag the DMFS scores of children malnourished earlier in childhood for age-rate analyses.

Acknowledgements

We would like to acknowledge the contribution to this study of Rudolph St. Jean, Project Coordinator; Dr Jerry Lowney, founder and Executive Director of the Haitian Health Foundation; Dr Ernst Joseph, Dean of the University of Haiti Dental School; and the key members of field team: Drs Elisandra Reyes and Germain Jean-Charles, NIH/NIDCR NRSA Postdoctoral Fellows at NYU;. Ms Ruthie Barrieau, an MS in Clinical Research graduate student at NYU, and Dr Butler Brice, a dentist in the Jeremie community. This study was supported by the grant NIH NIDCR R01 DE014708-01A2.

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