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SCIENTIFIC articles

Dental abnormalities in children with chronic renal failure

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Abstract

Abnormalities of dental enamel caused by disruption of normal dental development were found in a group of 17 children with chronic renal failure (CRF). Enamel hypoplasia was the most common abnormality, with discoloration and hypocalcification occurring less frequently. Hypoplastic enamel was noted in 11 of 17 subjects with CRF and in none of the control subjects, $p = .001$. Ten of 11 CRF subjects who had onset of advanced CRF (i.e., creatinine clearance ≤25 ml/min/1.73m^2) before age eight years demonstrated hypoplasia, $p = .002$. The teeth with hypoplastic enamel were those undergoing formation and mineralization at the time CRF became advanced. Less severe renal failure was not associated with enamel hypoplasia. Completely developed teeth were unaffected. Hypoplastic enamel on permanent teeth serves as a marker of the onset of advanced renal failure. In addition, children with CRF had few caries compared with healthy control subjects, $p = .004$.

Children with CRF manifest a multitude of systemic abnormalities which may include growth retardation and abnormal mineral metabolism. Although growth and bone mineralization have been studied extensively, there is a paucity of information concerning the effects of CRF on the mineralization and development of teeth. The present study was undertaken because abnormal teeth are a common finding in children with CRF who receive care in the Pediatric Nephrology Clinic of the University of Iowa Hospitals and Clinics. The study was designed to define the nature of the dental abnormalities, to assess the prevalence in the group studied, and to determine if the observed abnormalities could be related to the onset of advanced renal failure. The dental evaluation was begun as part of a general evaluation of nutritional status in childhood CRF and has been continued since completion of that evaluation.

Methods and Materials

Seventeen subjects were selected from a group of children with CRF attending the Pediatric Nephrology Clinic at the University of Iowa Hospitals and Clinics. All children over the age of five years with CRF and creatinine clearance less than or equal to 25 ml/min/1.73m^2 (advanced renal failure) were eligible. Etiology of the CRF was not a criterion for entry into the study.

Control subjects were recruited from staff families and, in one instance, from the siblings of a subject with CRF. Selection criteria included good health, normal growth, and no history of chronic illness. No attempt was made to match CRF and control subjects for age, sex, or size. The range of ages of the control and CRF subjects were the same.[a] Normal growth was defined as stature and weight greater than the tenth percentile for age. There were 10 control subjects, six boys and four girls.

The age at which renal failure was first diagnosed was determined by a review of the medical record of each subject. The criteria used by individual physicians to make the initial diagnosis of renal failure included serum creatinine and urea nitrogen concentrations, endogenous creatinine clearance, and various other clinical and biochemical alterations known to occur in renal failure. It should be remembered that the age at first diagnosis of CRF is not necessarily the age of onset of CRF.

The age at which advanced renal failure began was determined by chart review. In several instances children were already in advanced renal failure at the time of their initial evaluation and diagnosis. Since prior laboratory evaluation was not available for these children, the true age of onset of CRF could not be determined. In these cases the age of onset of advanced renal failure was arbitrarily defined as the age at which the initial diagnosis was made. Age is expressed in decimals (tenths

[a]The protocol was approved by the Human Use Review Committee of the University of Iowa before any subjects were enrolled. A complete explanation of the study was given to each subject and his or her parents and informed consent was obtained from the parents.

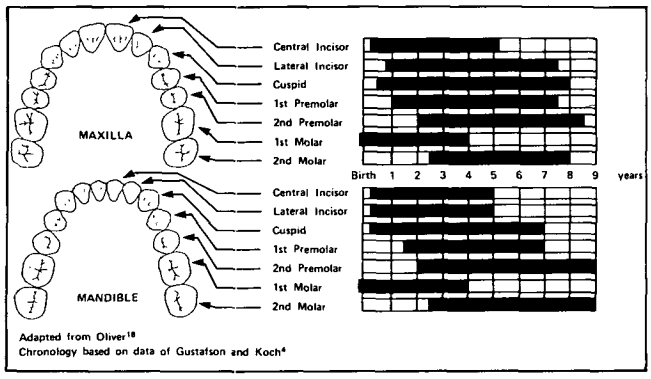

Figure 1. Chronology of formation of enamel for permanent teeth. The bars indicate the time period during which enamel is deposited and, consequently, is vulnerable to systemic stresses such as advanced renal failure.

of a year) rather than months.[1]

A comprehensive dental examination of each subject was performed by one of the investigators (A.N. or J.C.). Panoramic dental radiographs of all subjects were made. Periapical dental radiographs were taken when indicated. Enamel abnormalities were recorded photographically.

Enamel hypoplasia was said to be present if there were macroscopic defects in the enamel surface in the form of pits, furrows, or areas of absent enamel, corresponding to the defects described by Sarnat and Schour.[2] Hypoplasia was detected by direct examination of erupted teeth and by dental radiographic examination of unerupted teeth. The chronology of permanent enamel formation published by Gustafson and Koch[3] (Figure 1) was used to date the age at which enamel hypoplasia occurred.

Hypocalcification was assessed by direct examination, and was identified when chalky-white opaque areas were seen on normally contoured enamel.[4] The diagnosis of hypocalcification was restricted to teeth that did not have hypoplastic enamel.

Caries was identified and recorded. Tooth color was assessed visually. Discoloration was said to be present if the enamel color differed from normal (i.e., opaque white: primary; translucent yellow-white: permanent).[4] Characteristic discoloration (e.g., that of tetracycline) was sought and history of exposure to tetracycline obtained.

Data were analyzed using a 2 × 2 contingency table and X^2 test to detect differences between groups. All data were expressed as frequencies. The term significant is used throughout the paper to describe differences for which the p value was less than 0.05.

Results

A large proportion of children with CRF had abnormal dental enamel, and all healthy control children had normal enamel. Enamel hypoplasia was the most commonly noted abnormality of dental development and was limited exclusively to the group of children with CRF. Other abnormalities, including discoloration and hypocalcification were noted less frequently, but when identified, also were limited to the CRF group (Table 1). The presence of enamel hypoplasia in the CRF group and its absence in the control group was statistically significant, p = .001 (Table 1).

Dental caries was noted in both CRF and control groups, but the preponderance of caries was in the latter group (Table 1). This difference was statistically significant, p = .018.

The CRF group was subdivided into two groups based on the age at which advanced renal failure had its onset (Table 2). Eight years was chosen as the point of division between the subgroups, since enamel mineralization is essentially complete at this age for all but the extreme gingival area of the second permanent molars and the entire third permanent molars.[3] Those children having the onset of advanced renal failure before age eight years are labelled the early onset group; those having onset after eight years are identified as the late onset group.

Enamel hypoplasia was noted significantly more often in the early onset group than in the late onset group, p = .002 (Table 2). Only one subject in the late onset group had evidence of enamel hypoplasia: radiographs demonstrated hypoplasia of the third permanent molars

Table 1. Dental abnormalities in children with CRF and in healthy control subjects.

	CRF (n = 17)	Control (n = 10)	X^2	p
Enamel Hypoplasia	11	0	10.92	.001
Discoloration	7	0	5.56	.018
Hypocalcification	7	0	5.56	.018
Caries*	4	7	5.63	.018

CRF = Chronic Renal Failure, **Control** = healthy child,
X^2: Chi square based on 2 × 2 contingency table with 1 degree of freedom.
*Caries in primary and/or permanent teeth.

Table 2. Dental abnormalities in children with CRF related to the age at which creatinine clearance ≤25 ml/min/1.73m^2.

	Early Onset* (n = 11)	Late Onset + (n = 6)	X^2**	p
Hypoplasia	10	1	9.37	.002
Hypocalcification	7	0	6.49	.011
Discoloration	6	1	2.23	.129
Caries	2	2	0.50	.518

*Early Onset: ≤8 years, median age = 1.58 years; range: 0.07 to 6.47 years
+Late Onset: >8 years, median age = 9.65 years; range: 8.41 to 11.36 years
**X^2: Chi square based on 2 × 2 contingency table with 1 degree of freedom

and a hypoplastic band at the extreme gingival margin of the second permanent molars. No other subjects had sufficiently developed third molars to allow radiographic detection of hypoplasia.

The other abnormalities (discoloration and hypocalcification) were less frequent than hypoplasia and were found primarily in the early onset group. There was no significant difference in the occurrence of caries in the early and late onset group CRF subjects (Table 2).

The teeth on which hypoplastic enamel was identified were those which developed after creatinine clearance had fallen below 25 ml/min/1.73m^2. A period of gradual decline in renal function preceded advanced renal failure in five of the 11 early onset subjects and all of the late onset subjects. Teeth whose development coincided with the decline in renal function had normal enamel until creatinine clearance fell below 25 ml/min/1.73m^2, when hypoplastic enamel appeared. When development was completed before advanced renal failure developed, no hypoplasia occurred. Thus, the geographic location of hypoplastic enamel on permanent teeth corresponded to the age of onset of advanced renal failure.

Six children had advanced renal failure from early infancy and presented with the distribution of hypoplastic enamel shown in Figure 2a: permanent incisors, cuspids, and first molars were hypoplastic and the lesions were located on the incisal/occlusal surfaces of these teeth. Enamel formation of the involved teeth begins during the first few months of life[3] (Figure 1), hence, the insult that produced hypoplasia must have occurred at this time.

An insult later in the mineralization process produced the pattern of hypoplasia shown in Figures 2b and 2c: normal enamel on the incisal/occlusal surfaces of incisors and first molars, with hypoplasia of the mid portion of incisors and first molars, and of incisal/occlusal surfaces of cuspids, premolars, and second molars. The enamel affected by hypoplasia is normally mineralized during the period that extends from late in the first year of life into the third year[3] (Figure 1). Three subjects demonstrated this pattern and had onset of advanced renal failure during this time span.

The onset of advanced CRF between age 4.0 and 4.5 years produced the enamel hypoplasia shown in Figure 2d. As can be seen, there are bands of hypoplastic

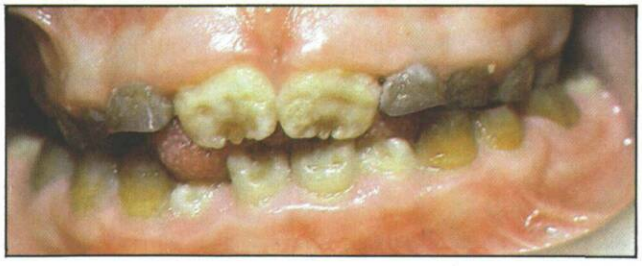

Figure 2a. Enamel hypoplasia of maxillary permanent central incisors and mandibular permanent central and lateral incisors noted in a boy age seven who had the onset of advanced chronic renal failure in early infancy. The entire enamel surface is hypoplastic on all affected teeth. Discolored teeth in this subject are primary teeth.

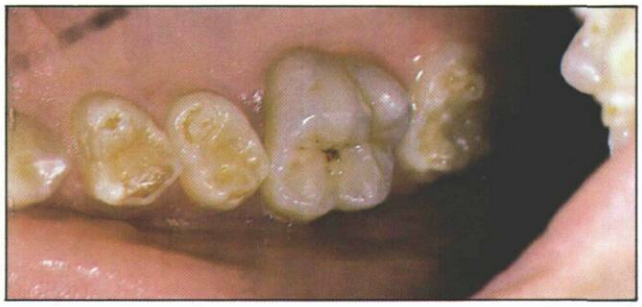

Figure 2c. Enamel hypoplasia noted in the subject described in Figure 2b. Maxillary first and second premolars and second permanent molar demonstrate total enamel hypoplasia. The first permanent molar has normal enamel except for a narrow band at the gingival margins.

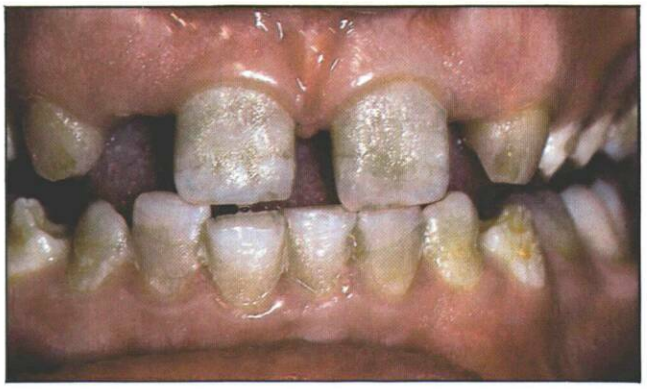

Figure 2b. Enamel hypoplasia noted in a 13-year-old boy who had the onset of advanced chronic renal failure between 1.5 and two years of age. Maxillary permanent central and lateral incisors and cuspids have normal enamel in the incisal ⅓ to ½, and hypoplastic enamel in the gingival ½ to ⅔. The mandibular first premolars are entirely hypoplastic. Maxillary lateral incisors are congenitally absent in this subject. Maxillary cuspids are primary dentition and demonstrate wear and extrinsic stain.

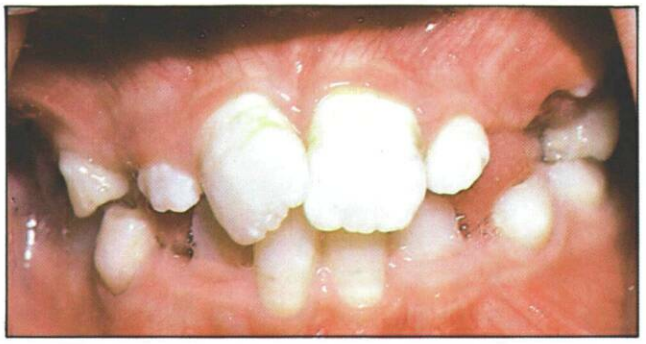

Figure 2d. Enamel hypoplasia noted in an 11-year-old boy who had the onset of advanced chronic renal failure between age 4.0 and 4.5 years. Bands of hypoplasia are evident near the gingival margins of maxillary and mandibular permanent central incisors.

enamel near the gingival margin of incisors. In addition, hypoplasia was noted at the gingival margins of first molars and in the midportion of premolars and second molars, though this is not visible in the illustration. This enamel mineralizes in the fourth year of life[3] (Figure 1), the time when this subject's renal function deteriorated.

The subject in the late onset group who was noted to have radiographic evidence of hypoplasia of the third permanent molars had advanced CRF onset between eight and nine years. The third molars develop after age eight.

Discussion

The relationship between CRF and enamel hypoplasia has not been reported previously in any detail. Stafne[5] published dental radiographs of an adolescent with CRF and osteodystrophy but he commented only on hypomineralization of bone and delayed root development. Bottomley et al.[6] mentioned that enamel hypoplasia occurs when CRF begins in early childhood but gave no supporting evidence. MacGibbon[7] reported a patient with renal failure and generalized enamel hypoplasia without comment on the etiology of the dental defects. Westbrook[8] included a photograph of an adolescent with enamel hypoplasia and CRF but made no specific or general comments. Chow and Peterson[9] described a child with CRF and commented on the presence of enamel hypoplasia, which they hypothesized was caused by "calcium deficiency" during dental development.

With the exception of the above case reports there have been no comments in the medical or dental literature about dental abnormalities in childhood chronic renal failure. CRF is not mentioned as a cause of enamel hypoplasia in a recent article which discusses etiology.[10]

Enamel hypoplasia is a relatively common phenomenon: Pindborg[11] notes that surveys have found hypoplasia of the permanent dentition in 3–15% of the general population; hypoplasia may be even more prevalent in certain undernourished populations.[10] Enamel defects reflect disruption of the process of enamel formation and mineralization during infancy and early childhood.

Tooth development is an orderly process that takes place over a limited time period. Enamel formation begins in utero for primary teeth at approximately the fourth month of gestation and continues for eight to 12 months postnatally. Permanent tooth enamel, excluding the third molars, is deposited during the period that begins shortly before birth and extends to approximately eight years (Figure 1).[3] Hypoplasia represents areas in which enamel has not formed because of disruption of the activity of ameloblasts, the enamel producing cells. Ameloblast activity begins at the incisal or occlusal surface of the crown and proceeds towards the gingival margin as individual ameloblasts differentiate and mature. Disruption of ameloblast activity by any systemic insult permanently affects all ameloblasts that would normally mature during the period the insult is active. Resumption of ameloblast activity occurs after the insult ceases, but a defect in the enamel, proportionate in width to the duration of the disturbing factor, remains.[2, 11]

Numerous systemic insults during infancy and early childhood produce enamel hypoplasia.[2, 10–12] Abnormalities of calcium metabolism including neonatal hypocalcemic tetany,[13–16] vitamin D deficiency rickets,[17] and nephrotic syndrome[18, 19] are known to result in hypoplastic enamel of permanent teeth. Nikiforuk and Fraser[10] demonstrated that hypocalcemia was the primary cause of enamel hypoplasia in the subjects they studied; hypophosphatemia was not associated consistently with enamel defects. The study of Nikiforuk and Fraser does not relate the age at which hypocalcemia occurred with the location of hypoplastic enamel on affected teeth.

Chronic renal failure is a major systemic insult to the growing child. Hypocalcemia is a prominent feature of CRF along with decreased serum levels of 1,25 dihydroxycholecalciferol (the active metabolite of vitamin D) and elevated serum inorganic phosphorus and serum parathyroid hormone levels. Bone growth and mineralization are disrupted as a result of the complex metabolic abnormalities present in CRF.[20] The data presented in this paper demonstrate that defective enamel growth and mineralization result when advanced chronic renal failure has its onset during dental development. In all likelihood enamel hypoplasia is the result of the same metabolic abnormalities that produce bone disease in children with CRF. However, the retrospective data available on the subjects reported in this paper are incomplete and do not allow comment on the relationship between hypocalcemia and enamel hypoplasia.

The low prevalence of caries in CRF subjects was striking. Dental caries is the most prevalent disease beyond infancy[21] with 90% of children having caries in permanent dentition by age 10 years.[22, 23] Yet, only 24% (4 of 17) CRF subjects have evidence of active caries. Caries resistance in CRF has been noted previously[9, 24] but the reason for this resistance has not been identified.

Implications

Enamel hypoplasia is a common, although under-reported, finding in children with CRF. Although the precise cause is unknown and cannot be determined from the data presented in this paper, the appearance of hypoplastic lesions on permanent teeth is related to decline in renal function. Regulation of calcium-phosphorus balance deteriorates when creatinine clearance falls below 25 ml/min/1.73m^2.[25] Thus, it is possible that disordered interactions among calcium, phosphorus, vitamin D, and parathyroid hormone may contribute to the production of enamel hypoplasia. If this is the case, careful attention to calcium supplementation, vitamin D replacement, and dietary phosphorus reduction — all of

which may prevent or diminish hyperparathyroidism — may decrease the severity of enamel hypoplasia.

It should be remembered that the process(es) causing enamel hypoplasia occurs years before the affected permanent teeth erupt and hypoplastic enamel becomes clinically evident. Thus, enamel hypoplasia is unlikely to be an aid in establishment of the diagnosis of CRF in a child; the diagnosis will have been made at an earlier age based on the metabolic abnormalities and growth failure that are the hallmarks of childhood CRF.

The disfiguring effect of enamel hypoplasia must be recognized. The burden of a chronic illness is made worse by visible signs of illness, especially those that adversely affect personal appearance. Consequently, the pedodontist should have an important role in the multidisciplinary team that shares responsibility for care of children with CRF. Patients and parents need to know that procedures exist whereby hypoplasatic enamel may be restored.[26] Of course, children with renal failure require routine dental care, too, although they are likely to have fewer caries than healthy children. The pedodontist on the renal team should provide that care or at least supervise the care provided by the family dentist.

Summary

Enamel defects reflecting disturbed dental development were prevalent in children whose creatinine clearance fell below 25 ml/min/1.73m^2 during infancy or early childhood. Lesser degrees of diminished renal function were not associated with enamel defects. Affected teeth were those for which developement was not yet complete at the time of onset of advanced CRF; no defects were noted on teeth for which development was already complete before renal function deteriorated. Enamel hypoplasia was the most common defect and its geographic location on permanent teeth corresponded to the age of onset of advanced renal failure. Although the relationship between enamel hypoplasia (as well as other dental developmental defects) and advanced CRF is well established from the data presented, the specific cause of enamel defects cannot be identified. It is likely, however, that disturbed mineral metabolism may well have an etiologic role.

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