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Differential Sensitivity in Growth and Development of Dental and Skeletal Tissue to Environmental Quality

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Dental and skeletal development provide a measure of physiological age that can be used to predict the optimal timing for treatment in orthodontic, orthopaedic or paediatric clinical practice or to estimate chronological age of child skeletal remains in forensic or archaeological contexts. Because the environmental sensitivity of skeletal and dental development can affect the ability to predict treatment timing and accuracy of age estimations, it is important to understand how these two tissues respond differently to environmental insults, such disease or malnutrition. This paper reviews the literature that supports the general assertion that dental development is less affected by environmental quality than skeletal development. It is concluded that the environmental sensitivity of tooth formation (compared to tooth eruption) has been rarely assessed and that there is a paucity of studies that examine the development of both tissues against socioeconomic and nutritional status or non-genetic disease.
Key-words: dental development; skeletal development; disease; nutrition; socioeconomic status.

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Determining the relationship between dental, skeletal and chronological age in children is fundamental for several disciplines, because it allows the researcher to understand variations in physiological or developmental age of children of the same chronological age. Since human growth shows a considerable variation in the chronological ages at which individual children reach similar developmental events, the developmental status of a child is best estimated relative to specific stages of physiological maturity (1). Some of the most common measures of physiological age rely on dental and skeletal maturation.

Several methods have been proposed for assessing dental maturation. One general approach focuses on the number and kind of teeth present in the mouth (2,3). Despite the simplicity of the approach there are some definite disadvantages because it relies on the timing of tooth emergence. Tooth emergence is a single, brief event in the continuous process of tooth eruption and the chance that the time of inspection coincides with the actual moment of emergence is, as a rule, small (4). The precision is also compromised by the fact that there are periods where no teeth erupt and others where several teeth erupt more or less simultaneously (5,6). In addition, tooth emergence may be influenced significantly by local exogenous factors, such as infection, obstruction, crowding, and premature extraction of the deciduous predecessor or adjacent permanent teeth (4,7-9). Most of the disadvantages can be avoided by using stages of tooth formation obtained from roentgenographic data on the calcification of teeth to determine dental maturity (10-14). Tooth formation is a progressive, continuous and cumulative process that ends only when tooth has been completely formed and is a measure of dental age that can be used throughout the entire growing period of an individual (5,15).

Skeletal development is commonly assessed by measuring skeletal maturity or, less frequently, by examining growth in height (skeletal growth). Skeletal maturity is usually derived from roentgenographic data on the appearance of centres of ossification, changes in size and shape of bones, and fusion or non-fusion of epiphyses of various skeletal structures, such as the hand or the knee. The most widely used standards are those developed by Greulich and Pyle (16) and by Tanner and co-workers (17) to assess skeletal age by osseous development of the hand and wrist. The greatest advantages advocated for these methods are their simplicity and availability of multiple ossification centres for the evaluation of maturity (18). Since skeletal maturation comprises changes in bone size and ossification of the growth plates it implies the completion of skeletal growth and height (19). Therefore, because these two developmental processes are closely related, growth in height can be used as a proxy for linear skeletal growth. Skeletal maturation however, is a better measure of biological maturation than height because any given skeletal age indicates how far a child has reached in the process of maturation, which terminates with fusion of all epiphyses and any given height does not indicate how great a percentage of its final height the child has attained, as the adult height is not known until the growth in length is completed (20).

Bone and teeth, however, have very distinct embryologic origins (21) and it is legitimate to assume that they differ in endocrine control and developmental sensitivity to environmental quality. The issue of which tissue (bone or teeth) is more sensitive to environmental insults during growth is important because it provides information on which maturation schedule (bone or teeth) to rely on to determine physiological and/or chronological age in paediatric, orthopaedic and orthodontic diagnosis and treatment, and in forensic investigations and anthropological research of past populations. The efficiency of the dental and skeletal system has been extensively tested in clinical settings for the prediction of the optimal timing of orthodontic, orthopaedic or paediatric treatment. The relationship between chronological, dental and skeletal age is used to assess delayed or advanced maturation for the application of the most suitable treatment or the clinical identification of pathological conditions (22-24). Comparatively, in forensic or anthropological studies the environmental sensitivity of dental and skeletal growth and development is essential to the accuracy of estimating chronological age of immature skeletal remains, because it relies on physiological age assessments. Usually, researchers assume, implicitly or explicitly, that teeth provide more accurate chronological age estimations than bone (25,26) and such a question of age accuracy is put aside in growth studies of past populations by assuming that the most useful comparisons of any group are between the two physiological indicators of maturation: dental age, which is more stable, and skeletal age, which is more sensitive to environmental insults (27).

It is generally assumed that dental development is not as affected by environmental influences as skeletal development, and such an assertion is supported by a number of sources. However, it is important to mention that these studies use different approaches to measure skeletal and dental development. For example, the greater proportion of studies that support the lesser environmental susceptibility of dental development focus on tooth emergence, rather than on tooth formation. The choice of assessment tool by different researchers may also influence the comparative maturity status assigned across populations. A study by Lewis and Garn (28) is one of the most cited sources that support the greater environmental sensitivity of skeletal development relative to dental development. These authors' goal was to understand variations in tooth formation and the relationship between tooth formation and general growth and development. They used roentgenographic data collected from the *Fels Longitudinal Growth Study* (Antioch College, Yellow Springs, Ohio) and found less variability, as assessed by the coefficient of variation, in dental development than in skeletal development. Tooth formation was less variable than tooth eruption, which in turn was less variable than skeletal maturation at the hand-wrist and the appearance of ossification centres. In a similar study, Demijian and coworkers (22) evaluated the interrelationships between somatic, dental, skeletal and sexual maturity in a longitudinal study of North American children and adolescents and found that peak height velocity was the most variable measure of maturity, followed closely by the appearance of the ulnar sesamoid, whereas tooth formation and menarche were the least variable measures. As with humans, dental formation in non-human primates (*Macaca nemestrina*) also shows less variability than birth weight or skeletal maturity, as measured by coefficients of variation (29).

Lewis and Garn (28) also found a weak correlation between the timing of permanent tooth formation and skeletal maturation, a result largely confirmed by several other studies (22,30-35). Although children advanced in height, weight, skeletal and sexual maturation tend to be advanced in tooth formation, correlations were low, rising somewhat at puberty. Green (23) and Lauterstein (33) obtained similar low correlations but also found that chronological age had a higher correlation with tooth formation, than measures of body size or skeletal maturation. Some studies, however, report high correlations between dental and skeletal maturity (36-39). Although some differences may derive from methodological issues, in all of these later studies the samples tend to be comprised of older children and adolescents, compared to the earlier studies. These disparities suggest some changes in the relationship between dental and skeletal tissue during the growth process. Overall, such findings are considered strong evidence in favour of independence between mechanisms controlling dental and skeletal maturation and, together with low variability in dental formation, are considered a strong support for closer genetic control over dental development than over skeletal development. In this context, several studies have shown that heritability of dental formation is high (40,41), whereas heritability of skeletal maturation (42) and growth in height (43) are lower. In addition, skeletal growth (growth in height) is more closely related to skeletal maturation than to dental development (22,23).

The lower sensitivity of dental development is also suggested by relative greater delays in skeletal maturation than in tooth formation in children with major abnormalities affecting growth, diseases and malnutrition. Vallejo-Bolaños and España-López (44) examined the developmental delay in dental and skeletal maturation of Spanish children with a growth disorder (short familial stature) and found that skeletal maturation was more retarded with respect to chronological age than permanent tooth formation. In turn, Ozerovic (45) examined the relationship between chronological age, dental formation and skeletal maturation in Yugoslavian children with cerebral palsy and reported that chronological and dental age differed on average by 1 to 7 months, while skeletal age differed from chronological age by an average of 4 to 11 months. In several cases of ß-thalassemia major, the mean delay in skeletal maturation was 28% compared to a mean delay of 17% in dental formation (46). Similarly, Garn and co-workers (47) reviewed a series of North American children with growth disorders of varying etiologies, including hypothyroidism, celiac disease and anaemia, and found that, in general, the degree of retardation in dental formation of this mixed group was approximately one-third the magnitude of the skeletal delay. Edler (6) arrived at very similar results in a sample of British patients with hypopituitarism, where average percentage delay in skeletal maturation was 27.9 % in age groups between 7 and 12 years, while for tooth formation, the average delay was only 9.3%. Keller and co-workers (48) also found that, compared to skeletal development, the dental system is not noticeably affected by endocrine and metabolic diseases, except in pituitary insufficiency, hyperthyroidism and delayed puberty.

The greater impact of nutrition on skeletal development is suggested by greater advancement of skeletal maturation relative to tooth formation in obese children (31). Another example of the impact of nutrition and of general improvement in living conditions is the study by Melsen and co-workers (49). These authors examined a group of Asian children, with inexact chronological age adopted by Danish families within one month after their arrival in Denmark and re-examined them one year subsequent to the first examination. At the time of the second examination the children showed an increment in dental age in accordance with the time interval between the two examinations but an increase in skeletal age that exceeded the corresponding time span. The authors suggest that the greater recovery of skeletal development reflected its greater environmental sensitivity. On the other hand, growth in height is more sensitive to nutritional effects than bone maturation (50,51). The lower sensitivity of dental maturation to nutritional effects is also suggested by the lack of a significant secular trend in tooth formation (52,53) in the presence of a substantial secular increase in height and advancement in skeletal maturation (54).

As expected, the differential effect of socioeconomic status on dental and skeletal development has also been used to support the assumption of greater environmental sensitivity of skeletal growth and maturation. However, studies that report socioeconomic differences in dental and skeletal development are rare and only examine tooth emergence and not tooth formation. Only two studies were found and are reviewed here. The first, by Garn and co-workers (55,56), examined the relative impact of socioeconomic differences on permanent tooth emergence and postnatal ossification in nearly 10,000 North American children between 4.5 and 16.5 years. Overall, the income-related delay in dental development was less than similarly observed for ossification timing. While the mean overall delay in tooth emergence between the low and high-income group was 0.098 years, the mean delay in skeletal maturation was 0.28 years. The bulk of the income influence on permanent tooth emergence, however, was in the male sample, with an average delay of 0.16 years. An analogous study by Low, Chan and Lee (57,58) examined a sample of Chinese children in Hong-Kong from three different socioeconomic backgrounds (high, middle and low). These researchers arrived at similar results. While the mean difference in eruption age between the high and low socio-economic groups was 0.23 years in males and 0.27 in females (57), low socio-economic status boys and girls were skeletally delayed by an average of 2.56 and 3.06 years relatively to the high socio-economic status group (58). In addition, a comparison of the three groups suggested that height was a better indicator of the socioeconomic influences than was skeletal maturation, since the differences in height between high and low socio-economic groups were much more significant (58). However, the delay in height was not provided. The relatively larger discrepancy in the difference between dental and skeletal development in the Low, Chan and Lee sample (57,58) compared to the one used by Garn and co-workers (55,56) may be related to the fact that there may have been larger socio-economic discrepancies in the Chinese sample than in the North American one. One important aspect of these studies is that because between-group comparisons are made within the same population, discrepancies between skeletal and dental age cannot be attributable to the use of specific standards.

Although there is considerable evidence that dental development is less susceptible to environmental influences, there is a paucity of studies that examine dental and skeletal development against socioeconomic and nutritional status or even disease, other than congenital or of genetic origin. The available studies rely mainly on tooth emergence and correlations with skeletal growth and maturation are usually carried out in controlled clinical settings, where examination of the potential effects of powerful environmental influences, such as malnutrition and chronic illness, cannot be carried out. In addition, the use of different methods to estimate dental and skeletal age may not help to completely clarify differences between dental, skeletal and chronological age. The issues discussed above suggest that the assumption of lower environmental sensitivity of dental development over skeletal development suffers from some problems and calls for a more systematic and comprehensive study of the differential impact of environmental factors, particularly socioeconomic conditions and nutrition, on the growth and development of skeletal and dental tissue. Is one relatively immune or are both affected? If so which one is more affected? And what is the difference in relative magnitude of the impact of external influences on bone and teeth? Are some aspects of skeletal and dental development more susceptible than others? For example, May et al. (59) examined the effects of nutritional supplementation upon bone and enamel development in a sample of rural Guatemalan children and found that formation of enamel responded positively to increased supplementation, while no differences in ossification were found between supplementation groups, suggesting that environmental effects may be more severe on intensity rather than on timing of dental development.

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