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Epidermolysis bullosa and dental developmental age

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Summary. *Objectives.* The dental development of permanent mandibular teeth in a small group of children with dystrophic epidermolysis bullosa (DEB) was assessed from radiographs and compared to a healthy, age-and-sex-matched control group.
Methods. This was a retrospective radiographic cross-sectional study. The sample consisted of a group of 44 children aged between 4 and 15 years with DEB and healthy, age-and-sex-matched controls. Two quantitative methods of assessing tooth formation were used: (1) a combination of information about tooth length and apex width; and (2) the use of tooth length to predict age. Panoramic radiographs were digitized in order to determine tooth length and apex width. Dental age was calculated, and the difference with real age was tested with Student's *t*-test.
Results. The dentition of both the DEB and control groups was slightly delayed. Using the first method, the delay was $0{\cdot}34 \pm 0{\cdot}87$ years for the DEB group and $0{\cdot}29 \pm 0{\cdot}97$ years for the control group. Using the second method, the delay was $0{\cdot}49 \pm 1{\cdot}18$ years for the DEB group and $0{\cdot}23 \pm 0{\cdot}62$ years for the control group. This delay was not statistically significant for either method.
Conclusions. The dental formation of permanent mandibular teeth in the group of children with DEB was not significantly different to that found in the control group.

Introduction

Epidermolysis bullosa (EB) is a group of diseases characterized by blister formation, and the major subtypes are classified by the level of ultrastructural cleavage [1,2]. The involvement of oral soft tissues and the enamel of developing teeth varies considerably [3]. The effect of EB on tooth formation and structure is unclear, and its clinical expression is highly variable [3]. Effects on enamel range from mild pit defects to severe hypoplasia, thin enamel or loss of enamel, especially in junctional types [3–15], although the chemical structure of the enamel is normal [16–18]. Dentine formation in all types of EB appears to be normal [5,11,13,19], although taurodontism has been documented [19]. The aim of this study was to assess the dental age of 44 children with dystrophic EB (DEB) and compare this to a healthy control group. Dental age was calculated using two quantitative methods based on measurements of tooth length and apex width from digitized panoramic radiographs [20,21]. This study was part of a collaborative investigation of maturation of the permanent dentition using one qualitative method [22] and two quantitative methods.

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Subjects and methods

The study group consisted of the 44 children detailed in Table 1. Rotational tomographs for the study group were collected from Great Ormond Street Hospital, London, UK, between 1992 and 1999. The control group consisted of the same number of healthy children, matched for age, sex and ethnic origin. The rotational tomographs for the control group were collected from the Eastman Dental Hospital, London, and the Royal London Dental Hospital, London, during 1999, and matched by age to within 3 months. All

Table 1. Age and sex of the sample: (SD) standard deviation.

Group	Number			Age (years)	
	Total	Girls	Boys	Range	Mean ± SD
Dystrophic epidermolysis bullosa	44	20	24	4·07–14·85	9·22 ± 2·43
Control	44	20	24	4·01–14·73	9·25 ± 2·44

Table 2. Prediction equations of method 1.*

Sex	Age range (years)	Prediction equation (age in days)
Boys	6–14	age = 3068 + 79·8 (tooth 47ARL) + 29·6 (tooth 44RL) – 182·3 (tooth 46AAW) – 24·7 (tooth 45AW)
	6–10	age = 2893 + 41·8 (tooth 47ARL) + 18·6 (tooth 43RL) – 104·5 (tooth 46AAW)
	8–12	age = 3186 + 53·8 (tooth 47ARL) – 108·6 (tooth 46DAW) – 44·6 (tooth 43AW) + 20·0 (tooth 43RL)
	10–14	age = 3835 + 62·5 (tooth 47ARL) – 91·5 (tooth 43AW)
Girls	6–14	age = 2902 + 67·1 (tooth 47ARL) + 37·3 (tooth 44RL) – 115·1 (tooth 46AAW) – 24·0 (tooth 43AW)
	6–10	age = 2817 + 42·0 (tooth 44RL) – 126·2 (tooth 41AW) + 33·4 (tooth 47ARL) – 69·0 (tooth 46AAW)
	8–12	age = 3358 + 37·7 (tooth 47ARL) + 22·6 (tooth 44RL) – 36·7 (tooth 43AW) – 110·6 (tooth 46DAW) – 36·7 (tooth 44AW)
	10–14	age = 3867 + 47·5 (tooth 47ARL) – 105·9 (tooth 47AAW) + 72·4 (tooth 48ARL)

*Dental age is the sum of the products after substituting the parameters into the equations (FDI notation of teeth). See the legend to Fig. 2 for abbreviations.

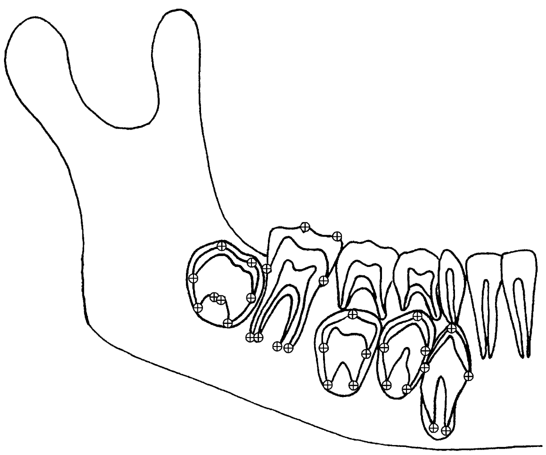

Fig. 1. Radiographic landmarks of the lower right mandibular canine, first and second premolars, and first and second molars. Reproduced with permission, Forensic Science International, Elsevier.

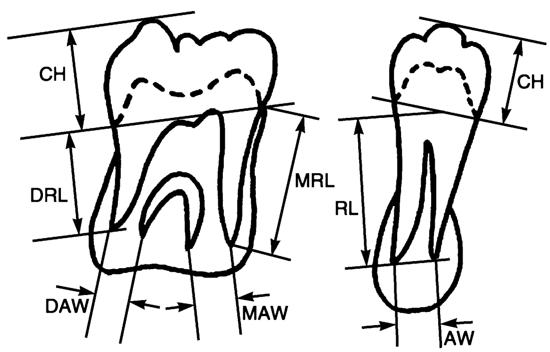

Fig. 2. Distances measured between defined landmarks: (CH) crown height; (DRL) length of distal root in molars; (MRL) length of mesial root in molars; (RL) root length of single-rooted teeth; (DAW) width of distal apex in molars; (MAW) width of medial apex in molars; and (AW) width of apex in single-rooted teeth. Reproduced with permission, Scandanavian Journal of Dental Research, Blackwell Munksgaard.

radiographs had been taken in the course of diagnosis and treatment.

Dental age was assessed from radiographs using two quantitative methods with the aid of a digitizer [23,24]. Radiographic landmarks of the lower right mandibular canine, the first and second premolars, and the first and second molars (FDI notation: 43, 44, 45, 46 and 47) were identified and the coordinates were recorded (see Figs 1 & 2). From these data, root length, crown length and apical width were determined for these teeth, and divided by the magnification factor 1·19 (Panelipse®). The radiographs used in this study were from several locations, and X-ray machines and details of differing magnification were not available. The resolution or the possibility of separating two points for this digitizer was set at 0·3 mm. Landmarks for each radiograph were identified, and data were only registered and saved by the digitizer if an immediate repeat sequence identification was within this resolution.

Table 3. Regression formulae for method 2.*

Tooth FDI	*b*0	*b*1	*b*2	*b*3	*b*4	*b*5
Canine 43	0·0644	0·2530	−0·0061	0·00962	−0·000724	0·0000147
First premolar 44	1·6140	0·5355				
Second premolar 45	2·2326	0·5604				
First molar 46	0·1258	−0·1992	0·1297	−0·00832	0·00017	
Second molar 47	0·1198	1·6049	−0·1141	0·00341		

*Age can be determined by measuring tooth length and substituting this value in the following equation:
$y = b0 + b1x + b2x^2 + b3x^3 + b4x^4 + b5x^5$,
where x is tooth length in millimetres and y is age in years.

Table 4. Intraobserver error: (SD) standard deviation.

Method	Number	Mean difference* (SD)
1	10	0·01 (0·18)
2	10	0·03 (0·11)

*Mean difference in dental age between the first and second reading.

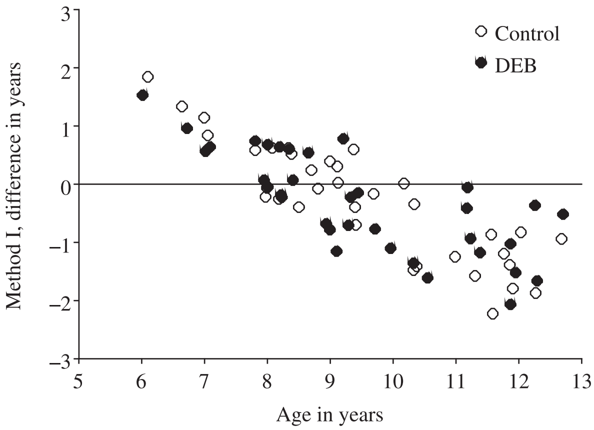

Fig. 3. Difference between dental age, assessed using method 1, real age.

Dental age was determined by substituting the calculated lengths and widths into the prediction equations for methods 1 and 2 (Tables 2 & 3). The real age of each child on the day of the X-ray was calculated by subtracting the date of X-ray from the date of birth after converting both to decimal age [25]. For each child, real age was subtracted from dental age and the difference was tested using Student's *t*-test.

Intraobserver error was calculated from 10 radiographs observed on two occasions (Table 4). The difference in dental age was tested using a *t*-test and found to be not statistically significant. For the group of children age from 8 to 12 years ($n = 27$), the regression equation for the 8–12-year-old age group was used [20], as shown in Table 2. For children aged outside this age interval, different regression equations were selected. Children younger than 6 years (five pairs) and older than 14 years (two pairs) were excluded from this part of the investigation. The other exclusions were children with missing teeth. Some were excluded from this part of the study; for others, an alternate regression equation was chosen. One child of the study group (9·18 years old) had missing permanent first molars, and this child (and the matched control child) was omitted from this part of the study since all equations for method 1 include this tooth.

Results

The results of the difference between dental age assessed using method 1 and real age are shown in Table 5 and Fig. 3. The average dental age for both the DEB and control groups was found to be slightly delayed, but this was not statistically significant. Figure 3 shows the difference between real and dental age for each child. A negative trend was apparent, with age being overestimated for younger children, underestimated for older children and most accurate around 8 years of age.

The results of the difference between dental age assessed using method 2 and real age are shown in Table 5 and Fig. 4. The average dental age for both groups was found to be delayed, but this was not statistically significant. Figure 4 shows the difference between the real and dental ages for each child plotted against age, and shows that the difference was least for children aged between 4 and 8 years. The most extreme outliers were in the older DEB group. Dental age for one boy aged 11·17 years was overestimated and it was underestimated in another boy aged 11·87 years. The results of the difference between dental and real age using individual teeth are found in Table 6. The tooth showing the least difference was the canine, although variance was high for all tooth types.

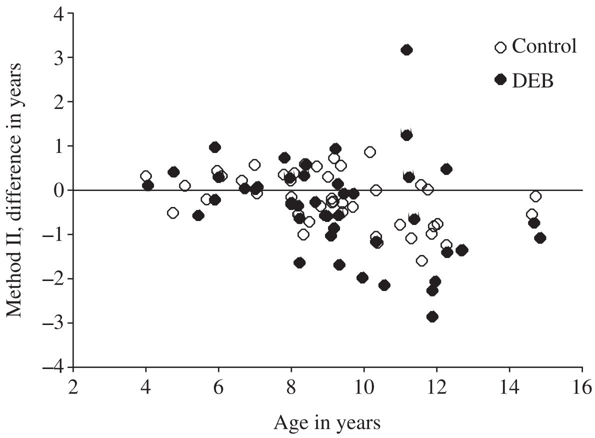

Fig. 4. Difference between dental age, assessed using method 2, real age.

Discussion

Several factors complicate the findings from this study and contribute to the variation seen in the results. Among these are the sample, the methods of assessing dental age, radiographic quality, and normal variation in tooth size and shape. The small sample of 44 children with DEB covers a wide age range (4·07–14·85 years), and the stage of the development of the dentition varies considerably between a child age 4 years and one aged 14. Many permanent teeth are developing at 4 years; at 14, only the roots are forming, if the third molar is excluded. Variation in dental development increases with age and this is evident in Figs 3 and 4. No information about the treatment or its duration was available for the DEB children involved in this study.

A number of methodological difficulties were encountered. Method 1 is based on the tooth parameters (crown height, apex width and root length) of Swedish children aged between 6 and 14 years, and gives a single age estimate from a combination of different developing teeth [20]. Method 2 is based on tooth length data from an excavated eighteenth-century coffin-buried population at Spitalfields, London [21]. Age is estimated from five permanent mandibular teeth as well as an average of the five teeth. This method was used for all subjects and for all available developing teeth. During the assessment of the X-rays with method 2, all mature teeth (closed apices) were omitted, and the average estimated age was calculating from the remaining teeth. For example, if the apex of the first permanent molar of a boy (10 years old) was radiographically closed, then this tooth no longer contributed to the development of the dentition, and dental age was calculated from the other developing teeth.

Measurements from radiographs rely on an undistorted image created by the correct positioning of the patient in the X-ray machine, and knowledge of the magnification factor. Mandibular tooth length measurements are reliable from good-quality rotational radiographs if the magnification is taken into account

Table 5. Results using both methods: (SD) standard deviation.

Group	Number	Mean age (± SD) (years) Dental	Mean age (± SD) (years) Real	Mean difference (SD)
Method 1				
Dystrophic epidermolysis bullosa	36	9·12 ± 1·24	9·46 ± 1·76	−0·34 (0·87)
Control	36	9·24 ± 1·01	9·52 ± 1·74	−0·29 (0·97)
Method 2				
Dystrophic epidermolysis bullosa	44	8·81 ± 2·32	9·22 ± 2·43	−0·40 (1·09)
Control	44	9·01 ± 2·22	9·25 ± 2·44	−0·23 (0·62)

Table 6. Results by tooth using method 2.

	Group			
	Dystrophic epidermolysis bullosa		Control	
Tooth FDI	Number	Mean difference (SD)	Number	Mean difference (SD)
Canine 43	43	−0·03 (1·54)	43	−0·06 (1·38)
First premolar 44	43	−0·47 (1·32)	42	−0·44 (0·71)
Second premolar 45	41	−0·28 (1·31)	43	−0·23 (1·02)
First molar 46	37	−0·54 (1·48)	34	−0·21 (1·09)
Second molar 47	44	−0·62 (1·37)	44	−0·23 (1·02)

[26–28]. The computer program used in this study was designed for Panelipse® (magnification factor of 1·19); however, the radiographs used in this study were from different X-ray machines. This might account for some of the variation in the results.

The sample used in this study was of mixed ethnicity. Method 1 is based on data from Swedish children [20]; it was tested on white Caucasian children in London and found to be most accurate around 8 years of age, decreasing in accuracy with increasing age [24]. This was also seen in the present study. The reason for this is unclear, and may be caused by population differences in both tooth formation and tooth length between Swedish and English children, although evidence suggests that population differences in tooth formation are inconsequential, and largely a result of sampling and methodology [29]. The prediction equations of method 2 are based on data from an excavated eighteenth-century coffin-buried population at Spitalfields, London [21]. This included very few individuals over the age of 5 years and may account for the large variation found for older children in both groups in the present study. In addition, the tooth length of fully formed unworn teeth is known to vary between individuals and sexes [30]. Using tooth length as a method to predict or assess age is hampered by the large variability in tooth length during formation. Further examination of the radiographs of several outliers in the EB group (method 2) seen in Fig. 4 show that one appeared microdont and another macrodont; this would account for the 'delay' or underestimated age. The stage of formation of developing teeth also varies between individuals at any given age [31] and it is reasonable to assume that a quantitative measure such as tooth length will show considerable variation at any given age during formation. This must be considered one of the limitations of the quantitative methods used in this study. Demirjian's method [32] is more readily available than having a digitizing program, but is not possible if teeth are missing. Both the qualitative and quantitative methods mentioned are similar in accuracy.

The main finding of this study is that tooth formation, measured using two quantitative methods, is slightly delayed in this small group of both children with DEB and healthy controls. The differences between the groups were not significant for either method. An expected result was the difference between real and dental age increasing with age, reflecting the known increasing variation in tooth formation with age. The slight delay is similar to that found in dental maturity using Demirjian's method [32] in this group of children ($P < 0{\cdot}05$, mean difference = 0·19 years, SD = 0·78) [22]. These findings support previous case reports and histological investigations suggesting that permanent tooth maturation proceeds as normal in children with DEB.

What this paper adds

- This paper describes a study of dental age in a group of children with Dystrophic Epidermolysis Bullosa (DEB) and a group of age and sex matched controls.
- Results suggest that dental age in patients with DEB may be little different to values seen in normal children.

Why this paper is relevant to paediatric dentists

- DEB may be associated with a variety of dental defects.
- Findings reported here are likely to be helpful to those planning dental care for affected children as well as assisting understanding of this disease.

Résumé. *Objectif.* Le développement des dents permanentes mandibulaires a été évalué, dans un petit groupe d'enfants avec épidermolyse bulleuse dystrophique (DEB), à partir de radiographies et comparé à celui d'un groupe d'enfants témoins appariés en âge et en sexe.
Protocole. Etude radiographique transversale rétrospective.
Echantillon. Groupe de 44 enfants (âgés de 4 à15 ans) avec DEB et témoins sains appariés en âge et sexe.
Méthodes. Deux méthodes quantitatives d'évaluation de la formation des dents ont été utilisées (Mörnstad *et al*. 1994; Liversidge, Molleson 1999). La méthode I combine les renseignements sur la longueur de la dent et la largeur d'apex et la méthode II utilise la longueur de dent pour prédire l'âge. Des radiographies panoramiques ont été numérisées afin de déterminer la longueur de dent et la largeur d'apex. L'âge dentaire a été calculé et la différence avec l'âge réel a été comparée à l'aide du test t de Student.
Résultats. La denture des deux groupes présentait un léger retard. Le décalage selon la méthode I était de 0,34 (± 0,87) ans pour le groupe DEB et 0,29 (± 0,97) ans pour le groupe témoin. Le retard selon la méthode II était de 0,49 (± 1,18) ans pour le groupe DEB et de 0,23 (± 0,62) ans. Ce décalage n'était pas statistiquement significatif quelque soit la méthode.
Conclusions. La formation des dents permanentes mandibulaires dans ce groupe d'enfants avec DEB

n'était pas significativement différente de celle d'enfants du groupe témoin.

Zusammenfassung. *Ziele.* Die Zahnentwicklung von bleibenden Unterkieferzähnen in einer kleinen Gruppe von Kindern mit dystropher Epidermolysis bullosa (DEB) wurde anhand von Röntgenaufnahmen ermittelt und mit Röntgenbildern einer Kontrollgruppe von nach Alter und Geschlecht gematchten Kindern verglichen.
Design. Retrospektive röntgenologische Querschnittstudie.
Stichprobe. Eine Gruppe von 44 Kindern mit DEB (Alter zwischen 4 und 15 Jahren) wurde mit einer nach Alter und Geschlecht gematchten Gruppe gesunder Kinder verglichen.
Methoden. Es wurden zwei Methoden der Zahnentwicklungsbestimmung benutzt: Methode 1 verbindet Informationen bezüglich Zahnlänge mit der Apexweite, Methode 2 benutzt die Zahnlänge zur Altersbestimmung. Panorama-Röntgenaufnahmen wurden digitalisiert um die Zahnlänge und Apexweite zu vermessen. Das Zahnalter wurde bestimmt und die Differenz zum tatsächlichen Alter wurde mittels t-Test analysiert.
Ergebnisse. Die Zahnentwicklung sowohl in der DEB-Gruppe als auch in der Kontrollgruppe erschien verzögert. Nach Methode 1 errechnete sich ein Wert von 0.34 (+/–0.87) Jahre für die DEB-Gruppe und 0.29 (+/–0.97) Jahre für die Kontrollgruppe. Nach Methode 2 lagen diese Werte bei 0.49 (+/–1.18) Jahren bzw. bei 0.23 (+/–0.62) Jahren. Die errechnete Verzögerung war bei keiner der beiden Methoden statistisch signifikant.
Schlussfolgerung. Die Zahnentwicklung bleibender Unterkieferzähne bei der untersuchten Gruppe von Kindern mit DEB zeigte keine deutlichen Unterschiede im Vergleich zu einer Kontrollgruppe.

Resumen. *Objetivo.* Se valoró el desarrollo de dientes inferiores permanentes en un pequeño grupo de niños con epidermolisis bullosa distrófica (EBD), a partir de radiografías y se comparó con un grupo control sano emparejados por edad y sexo.
Diseño. Fue un estudio transversal radiográfico retrospectivo.
Muestra. Grupo de 44 niños (entre 4 y 15 años) con EBD y uno control emparejados por edad y sexo.
Métodos. Se usaron dos métodos cuantitativos de valoración de la formación dentaria (Mörnstad *et al.* 1994; Liversidge, Molleson 1999). El método I combina la información de la longitud del diente y la anchura del ápice, el método II utiliza la longitud del diente para predecir la edad. Se digitalizaron radiografías panorámicas para determinar la longitud dentaria y la anchura del ápice. Se calculó la edad dental y se valoró la diferencia con la edad real mediante el test de la t de student.
Resultados. La dentición de ambos grupos, EBD y control, estaba ligeramente retrasada. El retraso usando el Método I fue de 0,34 (±0,87) año para el grupo de EBD y de 0,29 (±0,97) año para el grupo control. El retraso usando el Método II fue de 0,49 (±1,18) año para el grupo EBD y de 0,23 (±0,62) año para el grupo control. Este retraso no fue estadísticamente significativo para ningún método.
Conclusiones. La formación dentaria de los dientes permanentes inferiores en el grupo de niños con EBD no fue significativamente diferente del grupo de niños control.

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