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A GENETIC AETIOLOGY FOR SOME COMMON DENTAL ANOMALIES: A PILOT TWIN STUDY

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This pilot study investigated the aetiology of various dental anomalies. Twin-pair correlations were obtained for the total number of missing, ectopic, malformed and rotated permanent teeth which were scored from panoramic radiographs of 59 monozygotic (identical) and 42 dizygotic (non-identical) twin-pairs. All monozygotic (MZ) twin correlations were greater than the dizygotic (DZ) twin correlations, suggesting a significant hereditary aetiology. A familial history of such common dental anomalies could become a valuable asset in treatment planning.
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Key words: twins, genetic factors, dental anomalies.

Introduction

Previous studies have implicated a significant genetic aetiology for missing teeth,[1,2,3] malformed maxillary lateral incisors,[4,5] ectopic canines[6,7] and rotated teeth.[8,9] Early diagnosis of such impending dental anomalies via a positive family history, could significantly aid treatment planning.

The hereditary nature of missing teeth, as determined by combined prevalence and familial data[1,2] and also the study of twins,[3,10] is well documented. The extent of inheritance and the exact mode of transmission remains unclear.[11] A single autosomal dominant gene with incomplete penetrance has been suggested.[6] However, a familial tendency,[1,2] racial variation,[12] a female predilection,[11,13,14] an association with the number and size of the other remaining teeth[15,16,17] and other dental anomalies,[6,16,18,19,20,21] suggest a polygenic aetiology. Missing and malformed maxillary lateral incisors may however be due to a common gene.[4]

MZ-twin pairs can exhibit concordance with similar expression[22,23] and concordance with variable expression[24,25,26] for missing teeth. This fact points towards a multifactorial aetiology (that is, environmental factors in addition to the genotype, as causative factors).

Several aetiological factors for ectopic maxillary canines have been proposed. Labially positioned canines are thought to result from an arch length deficiency.[27] A lack of anatomical guidance due to malformed and missing maxillary lateral incisors has been implicated for palatally-positioned canines.[5,19] However, as with missing and some malformed teeth, racial variation,[7] female preponderance[7] and associations with other dental anomalies,[7,19,28] suggest a polygenic aetiology for palatally-positioned canines.

The aim of this pilot study is to compare the number of missing, ectopic, malformed and rotated permanent teeth between monozygotic (MZ) and dizygotic (DZ) twins. Correlations between MZ- and DZ-twins were calculated.

Materials and methods

Subjects

A total of 202 pre-treatment panoramic radiographs of 101 twin-pairs, 59 MZ (32 female pairs and 27 male pairs) and 42 DZ (14 female pairs, 14 male pairs and 14 opposite-sex pairs), were selected for this study. The mean age of the MZ-twins was 11.6 years (S.D.= 2.2 years with a range of 6.8 to 18.8 years). The mean age of the DZ-twins was 11.7 years (S.D.= 2.3 years with a range of 6.0 to 18.0 years).

Permission to use the dental radiographic records was obtained by written consent from the parents and an invitation to participate in a telephone questionnaire was issued to them. Radiographs for 74 of the 101 twin-pairs were obtained from local orthodontic practices and orthodontic records from The University of Queensland Dental School. The remaining 27 pairs of radiographs, which had been taken as part of an orthodontic evaluation, were provided from the East Flanders Prospective Twin Survey (EFPTS).*

Each twin-pair had radiographs taken with the same machine, and in 94 per cent of cases of each twin-pair, radiographs were taken on the same day. Twin-pairs with a known history of previous extractions, medical syndromes and those for whom any doubt about zygosity arose, were excluded from the study.

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Also omitted were twins whose radiographs were distorted due to positioning errors. Based on these exclusion criteria, 21 twin-pairs were rejected leaving a total of 101 twin-pairs for study.

Zygosity determination of the 27 twin-pairs from the EFPTS sample was carried out at birth by comparison of genetic markers examined on blood taken from the umbilical cord.[29] Serologic comparison of blood markers had been undertaken in seven of the 74 Queensland sample of twins. Zygosity determination for the remaining Queensland sample was based on review of responses to questions about physical similarity (a procedure which is accepted as being 95 per cent accurate),[30] and in 67 per cent of cases, examination of age-matched photographs which had been requested from the parents of the twins.

Each panoramic radiograph was assigned an identification number. Data collected for all of the twin-pairs included: gender, zygosity, method of zygosity determination and age at which the radiograph was taken. The radiographs were randomly scored for dental anomalies by a single examiner. They were inspected under optimal conditions using a masked illuminated viewer.

A permanent tooth was registered as missing when no tooth or tooth germ could be identified on the radiograph and the dental records confirmed that the tooth had not been extracted. A tooth was registered as ectopic when one of the following criteria was met:

1. It displayed an aberrant position or eruption path (with or without impaction);
2. It caused abnormal resorption of an adjacent deciduous or permanent tooth; and
3. Where a lack of space between adjacent erupted teeth indicated that an aberrant eruption path was likely.

A tooth was judged to be malformed when it displayed an unusual deviation from normal size or when the crown or root was dilacerated. Supernumerary teeth were also scored as malformed teeth. A tooth was judged to be rotated on the basis of its cuspal projection and pulpal appearance, provided no obvious positioning errors were apparent. Because of the age range of the twins, third molars were scored but were not

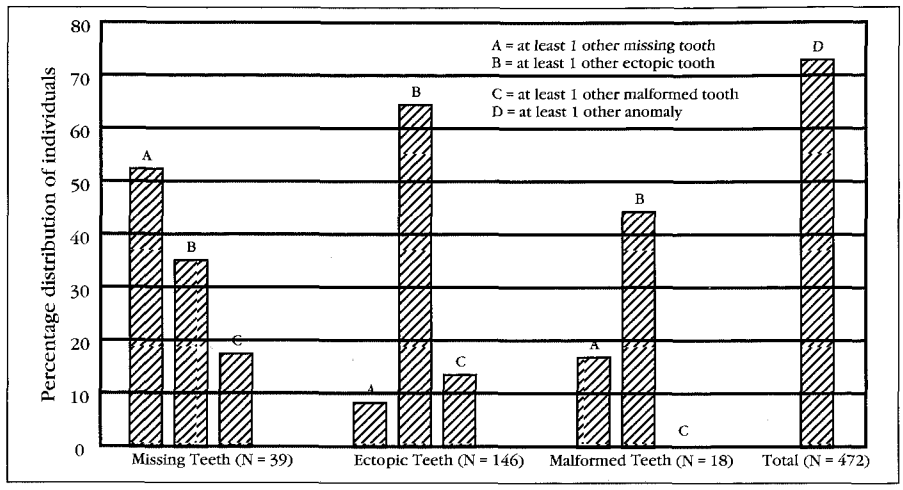


Figure 1. Percentage distribution of individuals with multiple and concurrent missing, ectopic and malformed teeth and multiple total anomalies (including rotated teeth).

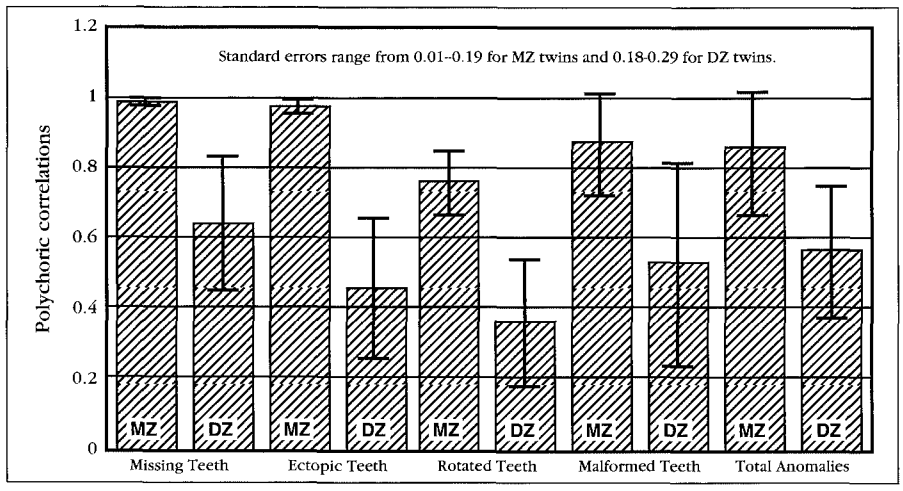


Figure 2. Polychoric correlations (± standard errors at the 5% probability range) for missing, ectopic, rotated and malformed teeth and total dental anomalies for MZ- and DZ-twins.

included in the analysis of the data. Twenty-nine twin-pairs were randomly selected and scored again two weeks later in order to determine the method error.

Data Analysis

Polychoric (phenotypic) correlations between MZ- and DZ-twin pairs were calculated using "Prelis2e" (Joreskog and Sorbom 1994).* Estimations of polychoric correlations implies that the distribution of dental anomaly scores obtained from inspection of radiographs, reflects an underlying liability for anomaly/trait expression that conforms to a continuous normal distribution. The polychoric correlations estimate the correlation between the underlying normally distributed latent variables; not the observed ordinal variables (Heath, Neale, Hewitt *et al* 1989).[31]

Genetic variation for the dental anomalies investigated may be evaluated by comparing correlations between MZ- and DZ-twin pairs. The twin model assumes that common environmental effects are similar for both MZ- and DZ-twin pairs; but the MZ-twin pairs have 100 per cent of their genes in common, whereas the DZ-twin pairs have on average only 50 per cent in common.

When MZ-twins resemble each other more than DZ-twins (rMZ > than rDZ), it may be inferred that genetics is playing a role. If the genetic effect is of the additive type and there is no effect of common environment, the MZ-twin correlation should be twice the DZ-twin correlation. If the MZ-twin correlation is greater than the DZ-twin correlation, but less than twice the DZ-twin correlation, a contribution of common environment in addition to additive genetics is implicated. When the MZ-twin correlation exceeds twice the DZ-twin correlation, evidence exists for non-additive genetic variance (that is, dominance and epistasis).

* "Prelis2e"© Joreskog KG, Sorbom D (1994): PRELIS: A preprocessor for LISREL, Mooresville, IN: Scientific Software International, Inc.

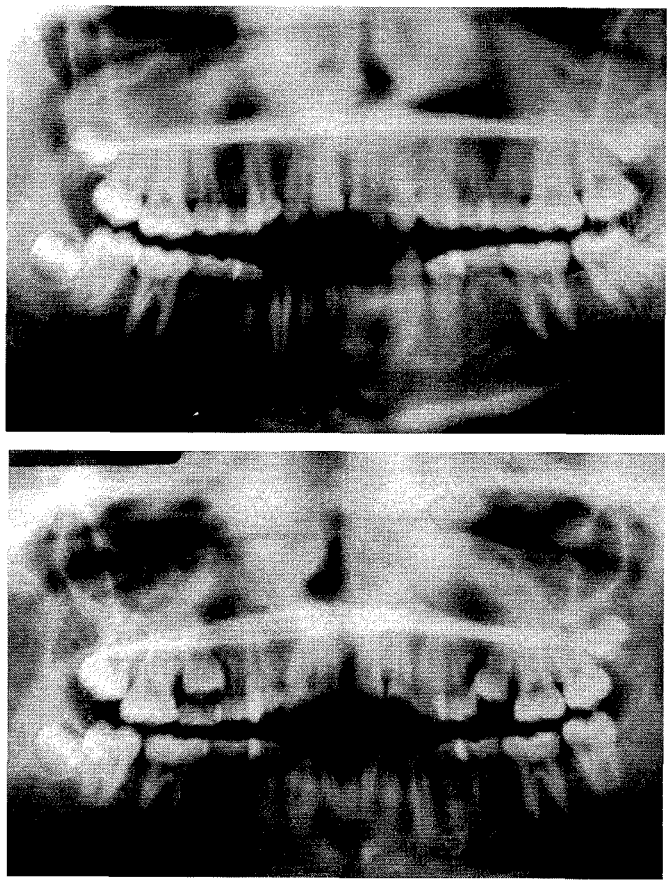


Figure 3. Concordance with similar expression for missing teeth (excluding third molars) in a pair of 13-year-old male MZ-twins. Both twins are missing mandibular right and left second premolars. Note, however, the variability with respect to third molars. The twin above has all third molars present, and the twin below has the maxillary right and mandibular left third molars missing.

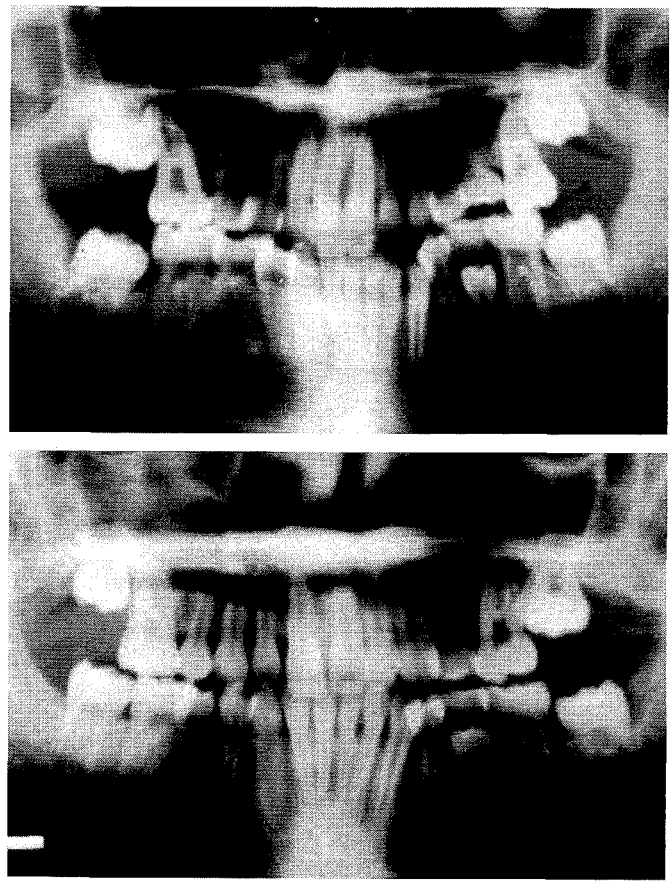


Figure 4. Concordance with variable expression for missing teeth in a pair of 13-year-old female MZ-twins. Both twins are missing maxillary right and left second premolars; however the twin above is also missing a mandibular right second premolar.

Results

Method error

Polychoric correlations for the intra-observer reliability were 0.96 for missing, 0.93 for ectopic, 0.93 for rotated and 0.96 for malformed teeth, all ($p<0.001$).

Distribution of anomalies

Of 202 individuals, 17 (8.4%) had a total of 39 missing teeth, 60 (29.7%) had a total of 146 ectopic teeth, 18 (8.9%) had a total of 18 malformed teeth and 117 (57.9%) had a total of 269 rotated teeth.

The most frequently missing teeth were: mandibular second premolars (30.8%), maxillary lateral incisors (23.1%) and maxillary second premolars (15.4%). Missing teeth were noted more frequently among females (88.2%), than among males (11.8%). This difference was highly significant ($p<0.001$). Missing teeth also occurred more often in MZ-twins (82.4%), than in DZ-twins (17.6%). This difference was significant ($p<0.05$).

Of the registered ectopic teeth, 43.1 per cent were maxillary canines and 30.1 per cent were maxillary premolars. Ectopic teeth were noted more frequently in the maxilla (80.8%), than in the mandible (19.2%). This difference was highly significant ($p<0.001$). Of the 63 ectopic maxillary canines, 36 were judged to be labially ectopic (associated with a lack of space between adjacent erupted teeth), fourteen were judged to be palatally ectopic (of which nine were impacted) and in thirteen cases the labio-palatal location could not be accurately ascertained without additional diagnostic information.

Peg-shaped and microdont maxillary lateral incisors comprised 61.1 per cent of the total malformed teeth. Maxillary midline supernumeraries and dilacerated teeth occurred in less than two per cent of all cases of malformed teeth.

There was no significant difference between left-hand side (53.1%) and right-hand side (46.9%) distribution of total dental anomalies, and they occurred more frequently in the maxilla (63.0%) than in the mandible (37.0%). This difference was highly significant ($p<0.001$).

Figure 1 shows the percentage distribution of individuals with multiple and concurrent missing, ectopic and malformed teeth, and multiple total anomalies (including rotated teeth).

Polychoric correlations

Figure 2 reveals that all MZ-twin correlations were greater than the DZ-twin correlations for the total number of missing, ectopic, malformed and rotated teeth, and also for the total dental anomalies. The pattern of MZ- and DZ-twin correlations indicates a significant hereditary aetiology for the dental anomalies investigated.

Concordance for exactly the same teeth missing, rather than total teeth missing, was evident in only two MZ-twin pairs. Similarly, concordance for exactly the same ectopic teeth, rather than total

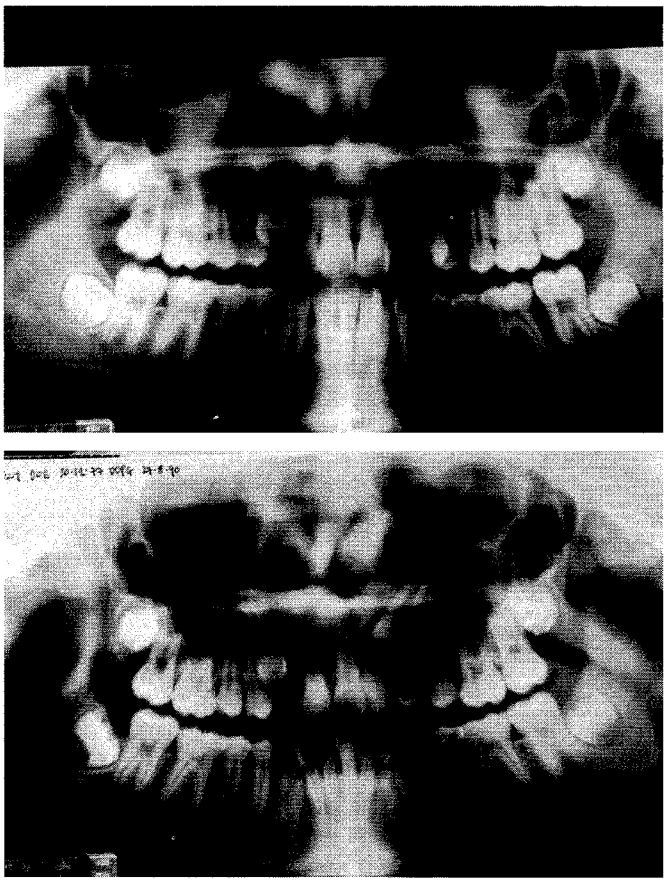


Figure 5. Concordance with variable expression for ectopic maxillary canines in a pair of 13-year-old female MZ-twins.

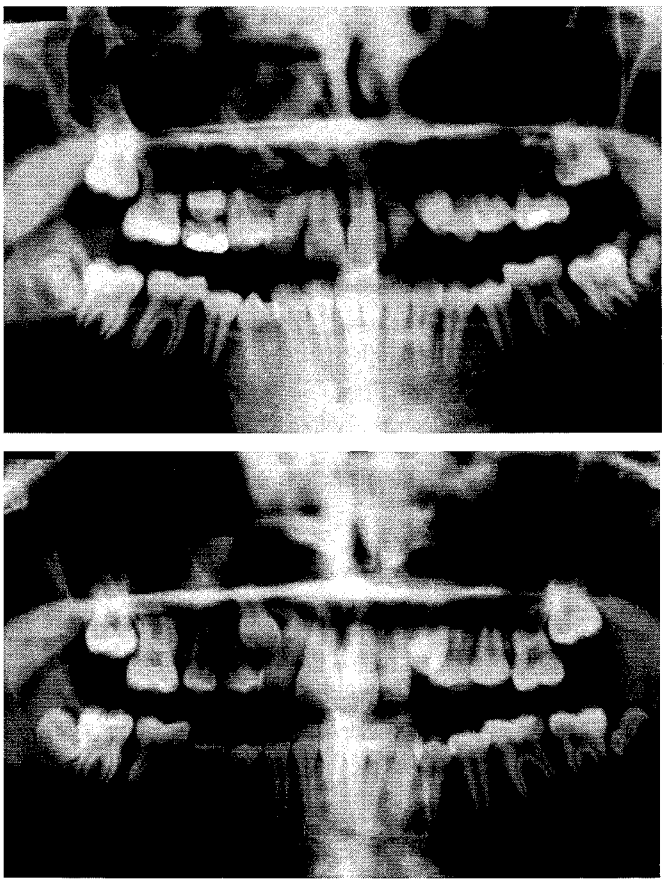


Figure 6. Concordance with similar expression for ectopic maxillary canines in a pair of 11-year-old female MZ-twins. Note also the concurrence of dental anomalies in the twin above, who also displays rotated maxillary left and mandibular right first premolars and a malformed maxillary left lateral incisor.

ectopic teeth, was noted in eight MZ-twin pairs and in one DZ-twin pair. Mirror-imaging of missing and microdont maxillary lateral incisors was apparent in one pair of MZ-twins.

Discussion

The prevalence of ectopic teeth in this study was 29.7 per cent. This is significantly greater than the 7.2 per cent prevalence of ectopic teeth reported by Bergstrom[32] in a radiographic investigation of a large random sample of schoolchildren. This difference may be explained by the fact that the twins in this study comprised an orthodontic sample and that ectopic teeth, as well as the other dental anomalies investigated, are often the reason for orthodontic referral and assessment.

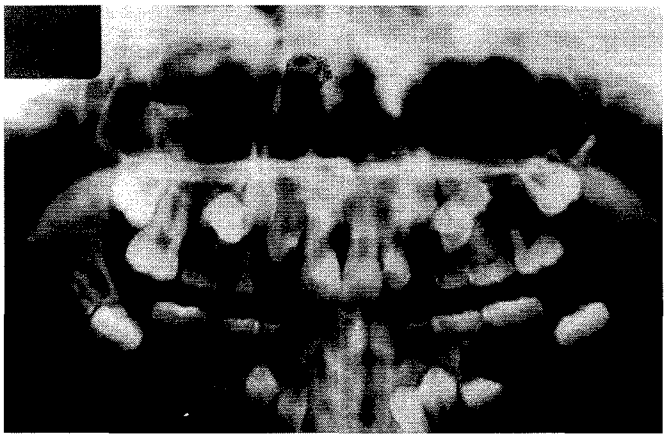
The frequency of occurrence of missing teeth in this investigation was 8.4 per cent. This compares with 8.5 per cent outlined by Markovic[3] who examined radiographs and plaster dental casts of 165 twin-pairs. In the present study, missing teeth occurred more frequently in MZ-twin pairs than in DZ-twin pairs ($p<0.05$). This finding is difficult to explain other than being due to sampling; however, Markovic[3] and (Townsend, Rogers, Richards *et al*)[33] have also reported a greater incidence of missing teeth in MZ-twin-pairs.

The findings pertaining to the most frequently missing teeth were consistent with previous studies;[16,20] however, it was noted that missing teeth occurred more frequently among females than among males ($p<.001$). A similar finding has been reported in other studies.[11,13]

According to the MZ- and DZ-twin correlations (Figure 2), the total number of missing teeth appears to be predominantly genetically controlled. Concordance with similar expression was evident in two out of eight MZ-twin pairs with missing teeth. Figure 3 illustrates an example.

Concordance with variable expression occurred in six out of eight MZ-twin pairs with missing teeth. Figure 4 provides an example. Concordance with variable expression for missing teeth in MZ-twins has been previously documented in other case reports.[24,25,26] This particular finding, along with the fact that the MZ-twin correlation is less than twice the DZ-twin correlation (Figure 2), highlights the possible role of environmental factors in addition to genotype with respect to the aetiology of missing teeth.

Figure 2 reveals that the total number of ectopic teeth has a significant additive genetic aetiology. Concordance with both similar and variable expression for ectopic maxillary canines (which comprised 43.1% of all ectopic teeth), was noted in six MZ-pairs and in one DZ-pair. Figures 5 and 6 illustrate examples of MZ-twins concordant for ectopic maxillary canines with variable and similar expression respectively.



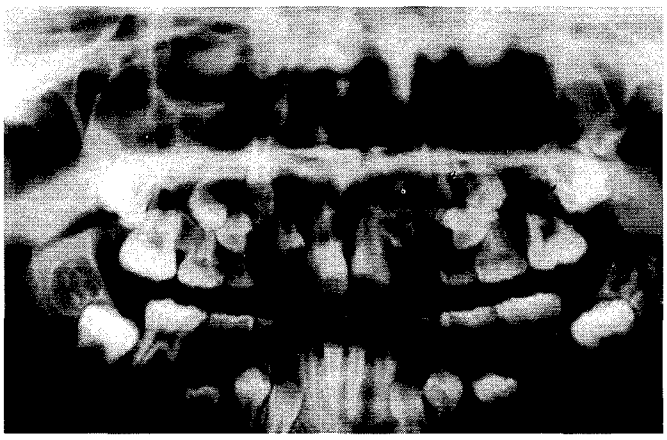
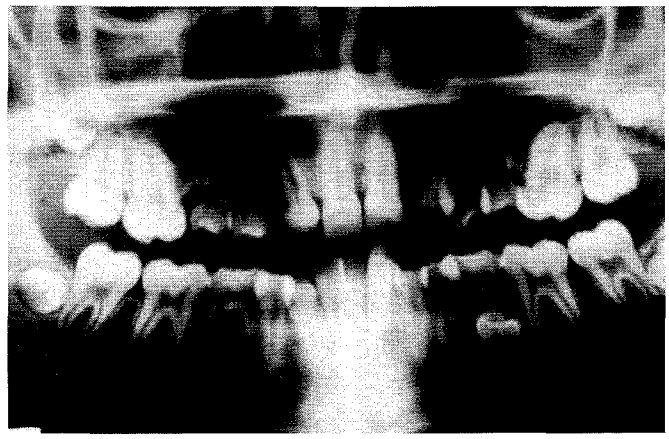


Figure 7. Concordance with similar expression for ectopic maxillary first and second premolars in a pair of 13-year-old male MZ-twins.



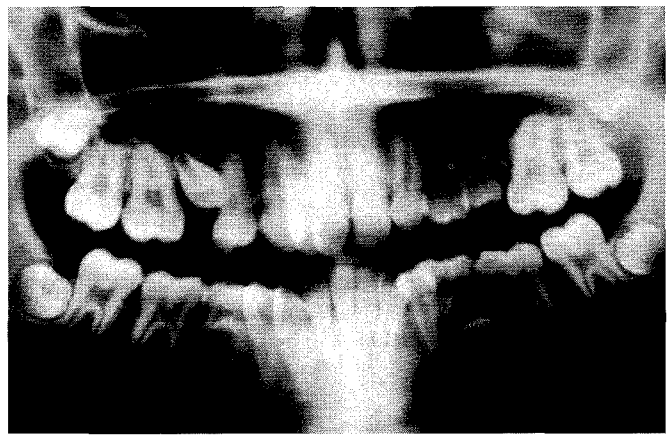


Figure 8. A pair of 12-year-old MZ females with concordance with variable expression for concurrent missing, ectopic and rotated teeth. Both twins have missing maxillary left lateral incisors and mandibular right second premolars; the twin above also has a missing maxillary right lateral incisor. The twin below has an ectopic maxillary right second premolar and mandibular left second premolar (also rotated). The twin above has a rotated maxillary left first premolar, and the twin below a rotated mandibular right canine.

To date, only family studies have been able to implicate a genetic mode of transmission for palatally-ectopic canines.[6] This study, based on the available diagnostic information, provides further evidence supporting the claim that the palatally-displaced canine may be a dental anomaly of genetic origin.[7] Moreover, it can similarly be proposed that labially-ectopic maxillary canines may also have an hereditary component in their aetiology.

While no control groups were available for direct statistical comparison, the incidence of association between missing, ectopic and malformed teeth in the same individual appears quite high (Figure 1). It has been speculated that a "common genetic defect" may give rise to the different phenotypic manifestations such as missing, malformed and even ectopic and malpositioned teeth. Those maxillary teeth which develop in the critical marginal areas of the dental lamina, such as the lateral incisors, canines and second premolars, seem the most susceptible.[6]

Evidence of such a "common genetic defect" becomes apparent by comparing the MZ- and DZ-twin correlations for the number of total dental anomalies in Figure 2. This association of dental anomalies is highlighted in Figure 8, which illustrates a pair of MZ-twins concordant with variable expression for concurrent missing, ectopic and rotated teeth.

The phenomenon of mirror-imaging for missing and microdont maxillary lateral incisors is shown in a pair of MZ-twin girls (Figure 9). Alvesalo and Portin[4] provide substantial evidence suggesting that missing and malformed maxillary lateral incisors are the result of a common gene. It was interesting to note that peg-shaped and microdont maxillary lateral incisors comprised 61.1 per cent of the total malformed teeth. The aetiology of mirror-imaging remains controversial as there is no evidence to rule out chance occurrence.[34]

Implications of this study

A familial history and early clinical or radiographic detection of one dental anomaly, could alert parents and clinicians of others impending in the same individual and also in other family members. Early diagnosis is important so that interceptive opportunities are not missed.

In patients with missing or malformed permanent teeth (the most common being maxillary lateral incisors and mandibular second premolars), mesial drift of permanent teeth can be promoted by interceptive extraction of deciduous teeth. This should apply only to those individuals demonstrating a favourable profile and growth pattern.

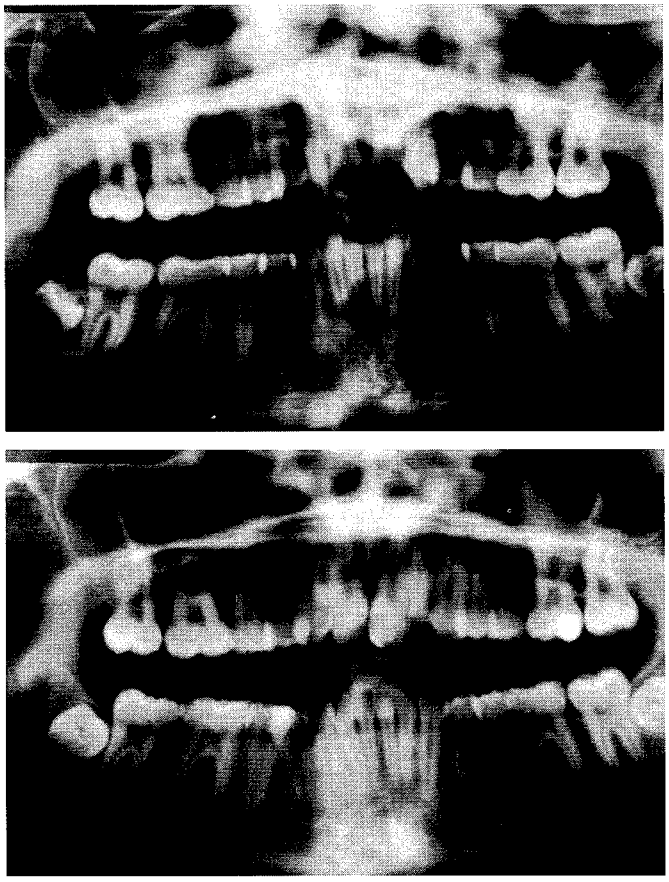


Figure 9. Mirror-imaging with respect to missing and microdont maxillary lateral incisors in a pair of 16-year-old female MZ-twins.

Selective removal of deciduous canines at the appropriate time may, in certain cases, allow the permanent canine to improve its ectopic palatal position without the need for future complex surgical and orthodontic retrieval.[35]

Determining the labio-palatal location of ectopic maxillary canines on the basis of relative magnification on a single panoramic radiograph can be difficult, particularly if these teeth are rotated.[36] Additional diagnostic information is often required.

Similarly, diagnosis of rotated teeth from panoramic radiographs is dependent upon the position of these teeth in the focal trough (the zone of maximum sharpness). Certain teeth such as the maxillary premolars may appear to be rotated, when in fact they are not.[37] Significant genetic variance for rotations and displacements of teeth has been demonstrated more accurately by examination of plaster dental casts of South Australian twins.[8]

Summary

The findings of this pilot study suggest that the total number of missing, ectopic, malformed and rotated permanent teeth has a considerable degree of genetic variation with respect to aetiology and apparent association. These findings, particularly with regard to the aetiology of ectopic maxillary canines, should encourage further studies of twins. Additional diagnostic information may help to clarify whether labial- and palatal-ectopic maxillary canines differ with respect to their aetiology.

Harris[38] in 1947 claimed: "The human jaws and teeth form an exceedingly complex unit; one which is considerably affected during growth by accidental or deliberate extrinsic factors. Nevertheless, it is probably true to say that no other unit of the human body lends itself so well to a quantitative and qualitative description of its complexities throughout the greater part of the life history of the organism. There is clearly an immense field of highly profitable research into human genetics here."

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