Volume 22, Number 1, 2009 ISSN 1096-9411

Dental Anthropology

A Publication of the Dental Anthropology Association

Dental Anthropology

Volume 22, Number 1, 2009

Dental Anthropology is the Official Publication of the Dental Anthropology Association.

Address for Manuscripts

Dr. Edward F. Harris
College of Dentistry, University of Tennessee
870 Union Avenue, Memphis, TN 38163 U.S.A.
E-mail address: eharris@utmem.edu

Address for Book Reviews

Dr. Greg C. Nelson
Department of Anthropology, University of Oregon
Condon Hall, Eugene, Oregon 97403 U.S.A.
E-mail address: gcnelson@oregon.uoregon.edu

Published at

Craniofacial Biology Laboratory, Department of Orthodontics
College of Dentistry, The Health Science Center
University of Tennessee, Memphis, TN 38163 U.S.A.

Strong genetic influence on hypocone expression of permanent maxillary molars in South Australian twins

Denice Higgins*, Toby E. Hughes, Helen James, Grant C. Townsend

Craniofacial Biology Research Group, School of Dentistry, The University of Adelaide, South Australia 5005

ABSTRACT An understanding of the role of genetic influences on dental traits is important in the areas of forensic odontology, human evolution and population variation. The aims of this study were: to calculate the frequency of occurrence and degree of expression of hypocones on permanent maxillary first and second molars in a sample of South Australian twins; to compare trait expression between males and females; to compare concordance rates for trait expression between monozygotic (MZ) and dizygotic (DZ) twins; and to fit genetic models to the data derived from twins and determine heritability estimates. Using stone dental casts, hypocone expression was scored on maxillary permanent first and second molars of 45 MZ twin pairs and 43 DZ pairs. Degrees of expression were scored from absence, through minor wrinkles or ridges, to very large cusps (score 0 – 5) using the standardized method of Turner *et al.* (1991). Hypocones were found to be more common and larger on first molars than second molars and there was a tendency for them to be larger in males although this was not statistically significant. No significant differences in occurrence or expression were noted between antimeres, with fewer differences observed between first than second molars. The percentage concordance for expression in MZ twin pairs was higher than in DZ twin pairs indicating a genetic influence determining the variation observed in hypocone expression. The most parsimonious model to explain observed variation was an AE model, incorporating additive genetic and unique environmental effects. Narrow-sense heritability estimates for both the first and second molars were high indicating that a large portion of the phenotypic variation could be explained by additive genetic effects. The greater range of phenotypic expression shown by the second molars compared with the first molars may reflect a common genetic liability that is modulated by differences in tooth size, location and/or developmental timing between these teeth. *Dental Anthropology* 2009;22(1):1-7.

A central focus of dental anthropological study over the last century or so has involved metric and non-metric analysis of the features of human teeth (Scott and Turner, 1977). The crowns of upper molar teeth have four main cusps and these are termed the paracone (mesiobuccal), protocone (mesiolingual), metacone (distobuccal), and hypocone (distolingual). Hypocone expression, like other non-metric dental crown traits, is generally scored by comparison with standardised plaques (Turner *et al.*, 2001). These plaques aid visual assessment of presence and degree of expression. In the context of phylogeny, dental characters are associated with functional demands and dietary adaptations but also reflect the developmental processes controlling morphogenesis.

The field theory that was proposed by Butler (1939) and adapted by Dahlberg (1945) in an attempt to account for the common features of teeth within a class, postulated that the most mesial tooth in each morphological class is usually the most stable phenotypically. Osborn (1978), in his clone theory, proposed that a single clone of pre-programmed cells led to the development of all teeth within a particular class. Both of these theories provide insights into the mechanisms that may be involved in patterning within the human dentition. Recent progress in studying these mechanisms at a molecular level indicates the involvement of homeobox-containing genes (Mitsiadis and Smith, 2006). Recently, Mitsiadis and Smith (2006) and Townsend *et al.* (2008) have proposed a new genetic developmental model for teeth that incorporates the field, clone and homeobox code theories.

Current evidence on development shows that tooth morphogenesis is punctuated by transient signaling centers in the epithelium, the primary and secondary enamel knots, corresponding to the initiation of tooth crowns and individual cusps (Jernvall, 2000). Differential growth and subsequent folding of the dental epithelium is directed by the enamel knots, which are composed of non-dividing cells. Cell proliferation around the

*Correspondence to: Dr Denice Higgins, Forensic Odontology Unit, School of Dentistry, Faculty of Health Sciences, University of Adelaide, 5005, South Australia. E-mail: denice.higgins@adelaide.edu.au

enamel knots is believed to be influenced by members of the fibroblast growth factor family. Genes involved in cusp development appear to be the same among all the individual cusps, with no particular gene for a single cusp, which means that at the level of molecular signaling, all the cusps are alike. A patterned cascade mode of cusp spacing may promote the evolution of new cusps and individual teeth may differ only in the timing of cusp initiation (Jernvall, 2000). As the secondary enamel knot program is repeated for every cusp, any small difference in cusp spacing will have a cumulative effect on later-developing cusps (Jernvall, 2000). Reflecting this concept, studies have shown that hypocones show the greatest variation in size of all upper maxillary molar cusps in hominoid primates and in humans (Jernvall and Jung, 2000; Kondo *et al.*, 2005).

Insight into the relative contributions of genetic and environmental factors to human tooth development can be gained from twin studies involving the comparison of monozygotic (MZ) and dizygotic (DZ) twin pairs. Differences between MZ twin pairs can be expected to be of similar magnitude to the minor left right differences that may be observed in singletons, whereas the differences between DZ pairs are similar to those seen in siblings (Kabban *et al*., 2001).

The purpose of this study was to investigate size variability of the hypocone of permanent maxillary first and second molars in a sample of South Australian twins. The specific hypotheses that were tested were:

- That hypocones occur more frequently and are larger in first molars compared with second molars
- That hypocones occur more frequently and are larger in males than females
- That hypocone expression is symmetrical between antimeric teeth
- That monozygotic twin pairs exhibit a higher degree of concordance for hypocone trait expression than dizygotic twin pairs, indicating a genetic contribution to observed variation.

MATERIALS AND METHODS

From a collection of dental casts of over 600 twin pairs, 45 MZ and 43 DZ pairs were selected. The twins were all of European ancestry and were aged between 10 and 46 years. Only individuals with permanent maxillary first and second molars present on both left and right sides were included. Subjects selected did not have any extensive restorations and their casts were not damaged. The study was approved by the Committee on the Ethics of Human Experimentation, University of Adelaide (Approval No. H/07/84) as part of an ongoing study of the teeth of Australian twins.

Hypocones were scored on right and left maxillary first and second molars using Turner's ASU classification system (Arizona State University System, Plaque 8) (Scott and Turner, 1997) with 6 grades of expression. Score 0 represented absence of a cusp, score 1 indicated a ridge or wrinkle present at the cusp site, score 2 was a faint cuspule, score 3 was a small cusp, score 4 was a large cusp and score 5 was a very large cusp. The casts were examined under a magnifying light and the degree of expression was determined by reference to a plaster replica of the scoring plaque. Assessments were made for all subjects on two separate occasions so that concordance rates between determinations could be calculated. A second observer scored 30 randomly selected casts for determination of inter-examiner reliability.

Statistical analysis was carried out using SPSS for Windows©. Frequencies were calculated for right and left side teeth, and for males and females. Associations between sides, first and second molars, and sexes were tested using chi-square tests. Statistical significance was set at an alpha of 0.05.

As a preliminary assessment of possible genetic influence on phenotypic expression, concordances rates were calculated for MZ and DZ pairs for all hypocone expressions. Structural equation modelling was then undertaken using the software package Mx (Neale *et al.*, 2006). Mx is a structural equation modelling package, flexible enough to fit a variety of mathematical applications. At its heart is a matrix algebra processor. There are many built-in fit functions to enable structural equation modelling (SEM) and other experiments in matrix algebra and statistical modelling, including facilities for maximum likelihood estimation of parameters from missing data structures, under normal theory. Complex 'non-standard' models are easy to specify. For further general applicability, it allows users to define their own fit functions, and optimization may be performed subject to linear and nonlinear equality or boundary constraints.

Mx can be used to apply structural equation models to variance-covariance matrices derived from monozygotic (MZ) and dizygotic (DZ) twin data. This method is particularly well-suited for continuously distributed data. However, SEM methodology can be extended to dichotomous and ordinal twin data by substituting the tetrachoric or polychoric correlation matrix (Pearson, 1901) for the variance-covariance matrix (Neale and Cardon, 1992). Use of SEM methodology for ordinal data is dependent on the assumption of an underlying continuous liability distribution that is bivariate normal. That is, it is assumed that categories are formed by imposing thresholds on a continuous liability distribution (Falconer, 1965; Reich et al., 1972).

Four sources of variation: A, additive genetic variance; D, non-additive genetic variance; C, common [shared] environmental variance; and E, unique [non-shared] environmental variance were modelled for twin pairs. A represents the additive effects of the alleles at a locus, whilst D refers to intralocus gene interactions.

C affects twin similarity regardless of zygosity, whereas E only represents unique effects contributing to within-pair differences.

Implicit in the model-fitting were the normal assumptions of the twin method: that mating was random; that trait-related, shared environmental influences on MZ and DZ twins were equal; and that there was no GxE interaction or gene-environment covariation (Jinks and Fulker, 1970). Since fitting models with four parameters to data from a classical twin study (MZ and DZ twins reared together) results in an under-identified model (Grayson, 1989; Hewitt, 1989; Dempsey *et al.*, 1999), subsets of three or fewer parameters were chosen.

Rectangular files of raw ordinal data were prepared as described by Neale *et al.* (2006) and utilized directly for univariate analyses of ordinal data, maximising the likelihood under a bivariate normal distribution model. For right and left first molars, scores of 3 or less were combined into a single category (*i.e.*, ≤ 3) as only one tooth was scored less than a 3. Starting values for model thresholds were estimated from raw frequencies.

When analysing raw data, there is no direct measure of goodness of model fit. Instead, nested sub-models can be compared by examining the log of the likelihood function (logL). Nested model differences in -2logL are distributed asymptotically as a χ^2, with degrees of freedom equal to the differences in free parameters between nested sub-models (*e.g.*, ACE *vs* AE = 1 df). Initially, a Cholesky decomposition of the data was undertaken to produce a saturated model fit against which to test goodness-of-fit of nested sub-models. Where models were not nested (*i.e.*, ACE *vs* ADE), the relative magnitude of the log of the likelihood was used to indicate the parsimony of each model. The general approach was that of accepting a more complex model only when a simpler one had failed. Path coefficients (a, c, e) were estimated. Heterogeneity of causes of variation between sexes was also evaluated.

Narrow-sense heritability estimates (h^2) were calculated from the ratio of genetic variation (A) to total phenotypic variation (A+C+D+E) in the best-fitting model. Values of heritability estimates near 1 indicate that most of the phenotypic variation can be explained by additive genetic effects whereas values near zero indicate that environmental effects account for most of the variation in the phenotype.

RESULTS

Concordance between the first and second sets of scores was 98% and there was no indication of systematic methodological errors. Inter-examiner concordance was 72% and the discrepancies found were generally of the order of plus or minus one category.

Hypocones were present on all permanent first molars and on a high proportion of second molars as demonstrated in Table 1. Pronounced expressions of hypocones were noted on first molars, with only one individual having a score of less than 3, and a high proportion of score 4 or 5. The second molars demonstrated more variation in hypocone expression. Subsequent genetic analysis treated hypocone expression on first molars as an ordinal trait with fewer categories than the second molars, yielding significantly lower power than the model for second molars, and consequently broader confidence intervals for parameter estimates.

Females had more pronounced expressions of score 4 and 5 on first molars, whereas the second molars showed more variability. Only 2% of females showed scores of

TABLE 1. Expression of hypocone trait in males and females (one member of each twin pair)[1]

	Males								Females							
	First molar				Second molar				First molar				Second molar			
	Right		Left		Right		Left		Right		Left		Right		Left	
Score	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
0	0	0.0	0	0.0	4	11.0	3	8.0	0	0.0	0	0.0	5	9.6	9	17.3
1	0	0.0	0	0.0	8	22.0	5	14.0	1	1.9	0	0.0	15	28.8	8	15.4
2	0	0.0	0	0.0	4	11.0	4	11.0	0	0.0	0	0.0	6	11.5	7	13.5
3	0	0.0	0	0.0	9	25.0	12	33.0	3	5.8	3	5.8	15	28.5	17	32.7
4	19	53.0	19	53.0	9	25.0	10	28.0	28	53.8	29	55.8	10	19.2	10	19.2
5	17	47.0	17	47.0	2	6.0	2	6.0	20	38.5	20	38.5	1	1.9	1	1.9

[1] n = 88

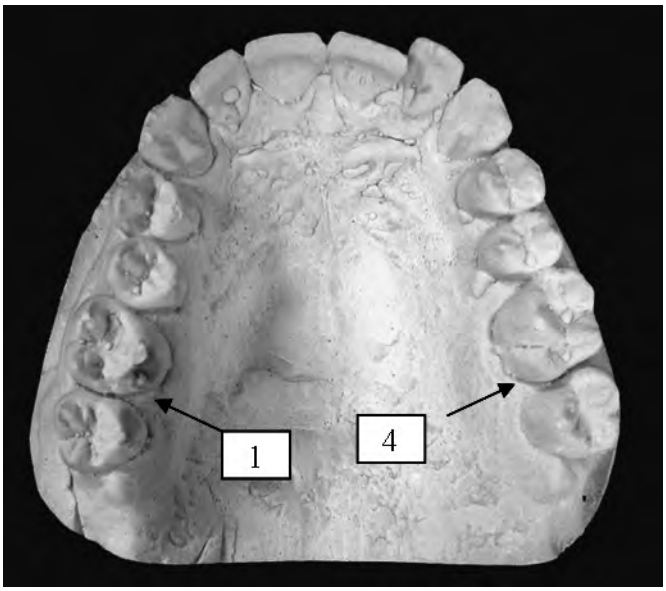

Fig. 1. Asymmetrical expression of hypocone trait on antimeric first molars—score 1 compared to score 4.

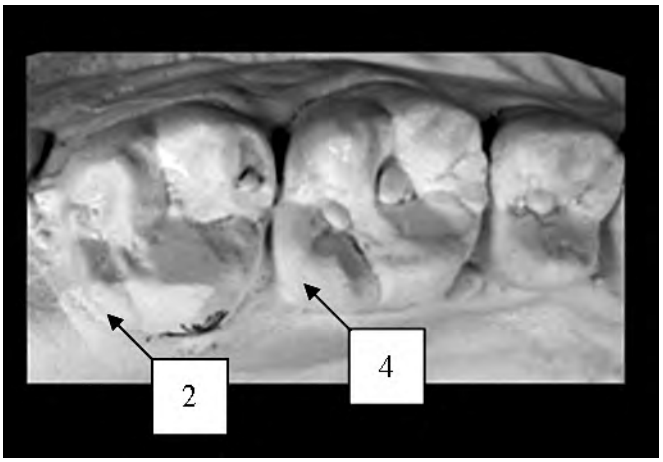

Fig. 2. Example of reduction in hypocone size from first to second molars—score 4 to score 2.

5 on both upper right and left second molars. Males showed a higher percentage of score 5 than females, with 47% of males showing score 5 compared to 38% of females. Females showed a higher percentage of score 4 and below. There was a tendency for male hypocones to be larger but this was not statistically significant.

In first molars, 98% concordance in expression between antimeric teeth was noted. The only example of marked asymmetry was one individual with score 1 on the left first molar and score 4 on the right first molar, as shown in Figure 1. In second molars, the concordance rate for antimeres was 74%.

The hypocone expression of first molars compared with second molars was examined in 88 individuals. One member from each of the 88 twin pairs (*i.e.* Twin A) was included in this analysis. As seen in Table 2, almost all of the scores for the maxillary right first molar were larger than those for the right second molar, except for five subjects—three had a score of 5 on both first and second molars, one had a score of 4 on the first molar and score 4 on the second, and one had score 3 on the first molar and score 4 on the second. When examining the maxillary left molars, again, most of the scores on the first molar were larger than those on the second molar except for four individuals—three had a score of 5 on both first and second molars and one had a score of

TABLE 2: Expression of hypocone trait on maxillary right first and second molars of individuals (one member of each twin pair)[1]

		First molars						
	Score	0	1	2	3	4	5	Total
Second molars	0	0	1	0	1	5	2	9
	1	0	0	0	1	17	5	23
	2	0	0	0	0	8	2	10
	3	0	0	0	0	16	8	24
	4	0	0	0	1	1	17	19
	5	0	0	0	0	0	3	3
	Total	0	1	0	3	47	37	88

[1]n= 88

TABLE 3. Percentage concordance observed for hypocone trait expression in DZ and MZ twin pairs

Tooth	Right M1	Right M2	Left M1	Left M2
DZ	67.4%	25.6%	67.4%	18.6%
MZ	80.0%	62.2%	80.0%	68.9%

4 on both first and second molars. A typical example of reduction in cusp size from the first to second molar is shown in Figure 2.

MZ twin pairs exhibited a higher concordance rate for corresponding tooth comparisons than DZ twin pairs, as shown in Table 3. Percentage concordance for the first molars between MZ twin pairs was 80% whilst that for DZ twin pairs was 67%. The concordance rate noted for the first molars was higher than that for the second molars, with the percentage concordance for the second molars being 65% for MZ twin pairs and 22% for DZ twin pairs.

An AE model was the most parsimonious for all variables. There was no significant heterogeneity between sexes for variance components for hypocone score. The final models represent pooled data from both sexes. As an example, Table 4 presents the pooled model structure and statistics for hypocone scoring of the upper right first molars only.

Table 5 presents narrow-sense heritabilities for hypocone score variability in the sample. All values were high and ranged between 0.87 and 0.93. The second molars had slightly higher estimates than the first molars.

TABLE 5. Narrow-sense heritability estimates (h^2) for hypocone expression of maxillary molars in Australian twins

Tooth[1]	h^2	L_1	L_2
Right first molar	0.87	0.65	0.96
Left first molar	0.87	0.67	0.97
Right second molar	0.90	0.80	0.95
Left second molar	0.93	0.86	0.97

[1]h^2 is heritability estimate; L_1 is lower 95% confidence limit of the h^2 estimate, and L_2 is the upper 95% confidence limit.

DISCUSSION

In this study, the 6-grade scoring method developed by Turner *et al.* (1991) for classifying hypocone expression was shown to be relatively easy to use and to provide consistent results. The intra-observer reliability of 98% was slightly higher than that of Takahashi *et al.* (2007) who reported a concordance rate of 92% for scoring categories of hypocone expression on two separate occasions. The inter-observer assessment study showed a concordance of 70-74% which was similar to that found by Nichol and Turner (1986) who recorded concordance between observers of 70-75% for ranked traits (error rate 25-30%).

The relative sizes of the cusps tended to correspond with phylogenetic and ontogenic timing of cusp formation. Apart from one case, the hypocone was shown to be reduced from the maxillary first to second molar. The one exception could possibly be due to different crown morphology making scoring difficult. The overall results were consistent with previous cusp area studies (Nichol and Turner, 1986; Macho and Moggi-Cecchi, 1992; Takahashi *et al.*, 2007) and support the morphogenic field concept of Dahlberg (1945).

As reported by Takahashi *et al.* (2007) this study did not show any statistically significant difference in the occurrence of hypocones between males and females. However, this may be a reflection on the categorical system of classification used, which gives little information about actual size variation. This study did, however, show a tendency for higher frequencies of larger hypocone expressions in males than females. Kondo *et al.* (2005) also reported that larger distal cusps were found in males rather than females. Hence, it is

TABLE 4. Genetic model structure and associated statistics for hypocone scores on the maxillary right first molar[1]

Parameterization	n	Parameters	-2 Log Likelihood	df	AIC
ACE	176	7	255.9	170	-84
ADE	176	7	256.0	170	-84
AE	176	6	256.0	171	-86
CE	176	6	260.8	171	-81
E	176	5	286.1	172	-58

[1] Abbreviations: n = sample size; df = degrees of freedom; AIC = Akaike's Information Criterion

likely that there is some influence of the sex chromosomes on the hypocone trait.

Hypocone expression was shown to be symmetrical between antimeric first molars except for one instance where the expression on the left was greater than the right, *i.e.* score 4 compared with score 1. A number of researchers have suggested that both sides of the dental arch are under the influence of common genetic factors (Potter *et al.*, 1976; Baume and Crawford, 1980). The findings of this study would support this hypothesis but the observed asymmetry in one individual would suggest environmental factors can lead to antimeric asymmetry.

The fact that this study shows a lower rate of concordance for hypocone expression between right and left maxillary second molars than first molars relates well to the schedule of tooth development and the theory that there is an association between early crown formation and low morphological variation of the first molar (Macho and Cecchi, 1992). These findings support the contention that certain teeth in the dentition, generally the earlier-developing members of each tooth class, are under stronger genetic control than later-forming teeth that are more subject to environmental influences (Corruccini and Potter, 1981).

It is assumed that MZ twins share 100% of their genes but the similarities between them can be due partly to shared pre- and post-natal environment (Scott and Turner, 1997). Common environment is perfectly correlated between twins in both zygosity groups whereas unique or non-shared environment only contributes to differences between twins. If genes are responsible for the expression of a trait, then a higher concordance of expression between MZ twin pairs would be expected compared with that seen between DZ twin pairs. This is what was noted in this study. However, although the concordance rate of expression of hypocones in MZ twin pairs was higher than that in DZ twin pairs, the concordance was not 100%.

Narrow-sense heritability estimates indicate the proportion of the phenotypic variation attributable to additive genetic effects. Narrow-sense heritability is a measure of the degree to which individual phenotypes are determined by genes passed from parents to offspring, expressed as the ratio of the additive genetic variance to the total phenotypic variance. The high heritability estimates noted in this study suggest that most of the variation in expression of hypocones is due to genetic influences but environmental factors can still contribute to the observed variation. Hypocones were universally present on first molars; the second molars demonstrated a greater range of phenotypic expression than the first molars, with absence noted in some individuals. This may suggest that there is a common genetic liability for hypocone expression on both the first and second molars, which is modulated by differences in size, location and/or developmental timing events between these teeth.

In studies aimed at disclosing patterns in estimates of heritabilities, it has generally been assumed that the highest heritability will be displayed by the key tooth in each morphogenetic field (Townsend *et al.*, 2008). This was not noted in this study; in fact, slightly higher values were achieved by the second molar compared with the first. It is considered that the longer a cusp remains in its soft tissue stage prior to mineralisation the more likely phenotypic variation will occur since odontogenesis involves a series of complicated epigenetic and morphogenic events. (Townsend *et al.*, 2008). Due to the relatively small variation in hypocone size on the first molars, only three categories were analysed (score 3 and below, score 4 and score 5), whereas when looking at second molars all six categories were considered. This difference in the categories of expression analysed between the first and second molars may have influenced the heritability estimates, contributing to the lower scores noted for the first molars.

CONCLUSIONS

The hypotheses of this study were generally supported in that:

1. Hypocone expression was more common and larger in maxillary first molars than second molars.
2. Although sexual dimorphism was not statistically significant, there was a trend for males to have larger scores than females.
3. The expression of hypocones was symmetrical between antimeric teeth, with the concordance rates between sides being higher in first molars than second molars.
4. Monozygotic twin pairs exhibited a higher concordance rate hypocone expression than dizygotic twin pairs.

The results of model fitting and calculation of heritability estimates indicated that genetic factors exert a strong influence on hypocone expression in human maxillary molar teeth but environmental factors can also contribute to observed variance.

ACKNOWLEDGEMENTS

The authors would like to particularly acknowledge Dr Zaliha Ismail, who initiated this project but sadly was unable to see it through to publication. We also acknowledge the Minister for Police in South Australia and the South Australian Police. This study also forms part of an ongoing investigation of the teeth and faces of Australian twins and their families that is supported by the National Health and Medical Research Council of Australia and the Australian Dental Research Foundation. The authors would like to thank the twins and their families who have agreed to participate in this research project and the Australian Twin Registry for their continuing assistance.

LITERATURE CITED

Baume RM, Crawford MH. 1980. Discrete dental trait asymmetry in Mexican and Brazilian groups. Am J Phys Anthropol 52:315-321.

Butler PM. 1939. Studies of the mammalian dentition. Differentiation of the post-canine dentition. Proc Zool Soc of London 109:1-36.

Butler PM. 1956.The ontogeny of molar pattern. Biol Rev 31:30-70.

Corruccini RS, Potter RHY. 1981. Developmental correlates of crown components asymmetry and occlusal discrepancy. Am J Phys Anthropol 55:21-31.

Dahlberg A. 1945. The changing dentition of man. J Am Dent Ass 32:676-690.

Dempsey PJ, Townsend GC, Richards LC. 1999. Increased tooth crown size in females with twin brothers: evidence for hormonal diffusion between twins in utero. Am J Hum Biol 11:577-586.

Falconer DS. 1965. The inheritance of liability to diseases estimated from the incidence among relatives. Ann Hum Genet 29:51-75.

Grayson DA. 1989. Twins reared together: minimizing shared environmental effects. Behav Genet 19:593-604.

Hewitt JK. 1989. Of biases and more in the study of twins reared together: a reply to Grayson. Behav Genet 19:605-608.

Jernvall J. 2000. Linking development with generation of novelty in mammalian teeth. Proc Natl Acad Sci USA 97:2641-2645.

Jernvall J, Jung HS. 2000. Genotype, phenotype and developmental biology of molar tooth characters. Am J Phys Anthropol 31:171-190.

Jinks JL, Fulker DW. 1970. Comparison of the biometrical genetical, MAVA, and classical approaches to the analysis of human behaviour. Psychol Bull 73:311-349.

Kabban M, Fearne J, Jovanovski V, Zou L. 2001. Tooth size and morphology in twins. Int J Paediatr Dent 11:333-339.

Kondo S, Townsend GC, Yamada H. 2005. Sexual dimorphism of cusp dimensions in human maxillary molars. Am J Phys Anthropol 128:870-877.

Macho GA, Moggi-Cecchi JM. 1992. Reduction of maxillary molars in *Homo sapiens sapiens*: a different perspective. Am J Phys Anthropol 87:151-159.

Mitsiadis TA, Smith MM. 2006. How do genes make teeth to order through development? J Exp Zool 306b:177–182.

Neale MC, Boker SM, Xie G, Maes HH. 2006. Mx: statistical modeling. VCU Box 900126, Richmond, VA 23298: Department of Psychiatry, 7th ed.

Neale MC, Cardon LR. 1992. Methodology for genetic studies of twins and families. Dordrecht, The Netherlands: Kluwer Academic Press.

Nichol CR, Turner CG II. 1986. Intra- and interobserver concordance in observing dental morphology. Am J Phys Anthropol 69:299-315.

Osborne JH 1978. Morphogenetic gradients: fields versus clones. In: Development, function and evolution of teeth. Butler PM and Joysey KA editors. New York: Academic Press. p 171-201.

Pearson K. 1901. Mathematical contributions to the theory of evolution. VII. On the correlation of characters not quantitatively measurable. Philos Trans R Soc Lond Ser A 195: 1-47.

Potter RH, Nance WE, Yu PI, Davis WB. 1976. A twin study of dental dimension. II. Independent genetic determinants. Am J Phys Anthropol 44:397-412.

Reich T, James JW, Morris CA. 1972. The use of multiple thresholds in determining the mode of transmission of semi-continuous traits. Ann Hum Genet Lond 36: 163-183.

Scott GR, Turner CG II.1997. The anthropology of human teeth. Cambridge: Cambridge University Press.

Takahashi M, Kondo S, Townsend G, Kanazawa E. 2007. Variability in cusp size of human maxillary molars, with particular reference to the hypocone. Arch Oral Biol 52:1146-1154.

Townsend G, Harris EF, Lesot H, Clauss F, Brook A. 2008. Morphogenetic fields within the human dentition: a new, clinically relevant synthesis of an old concept. Arch Oral Biol doi:10.1046/jarchoralbio.2008.06.011.

Turner CG II, Nichol CR, Scott GR. 1991. Scoring procedures for key morphological traits of the permanent dentition: the Arizona State University dental anthropology system. In: Advances in dental antropology. Kelly MA, Larsen CS, editors. New York: Wiley-Liss. p 13-31.

Patterns of Hypodontia among Third Molars in Contemporary American Adolescents

Edward F. Harris*

Department of Orthodontics, University of Tennessee, Memphis, Tennessee

ABSTRACT: Third molars (M3s) are congenitally absent (hypodontic) more frequently than any other tooth type. Causes of this enhanced variability are poorly understood, but the potential range of absence—from none through four M3s per person—provides the opportunity to examine the permutations of missing M3s within and among ethnic groups. Teenage samples of two overlapping populations (1,100 American whites; 600 American blacks) were studied here, with radiographic confirmation of each tooth's presence in the jaws. Roughly 15% of these people are missing at least one M3, but only about 2% of this sample is hypodontic for all four molars. The frequency and severity of missing M3s are significantly higher in whites than blacks. Within individuals, correspondence of occurrence is much higher within than between the jaws, but all combinations of M3 hypodontia are positive and significant statistically—implying common underlying developmental influences. While various sorts of data support a genetic influence on the risk of M3 hypodontia, patterns of inheritance suggest a multifactorial rather than a single-gene mode of inheritance. Several researchers have promoted a polygenic threshold model, and the history and application of this model are discussed. *Dental Anthropology* 2009;22(1):8-17.

Hypodontia—the congenital absence of a tooth—is not uncommon in contemporary human populations. Evidence suggests that the risk and pattern of missing teeth are under some genetic control, and it is evident that frequencies differ between sexes and among races. By far, the tooth type most likely to be congenitally missing in contemporary humans is the third molar (M3). Nanda (1954), Eidelman *et al*. (1973), Thompson *et al*. (1974), Mattheeuws *et al.* (2004) and Polder *et al*. (2004), among others, have reviewed M3 frequencies in contemporary human populations.

Various speculative ideas have been put forth to explain how a tooth can be congenitally absent and, in particular, why M3s commonly are missing (see, *e.g*., Pindborg, 1970). These mechanistic ideas predate a modern understanding of molecular signaling in tooth development (*e.g*., Matalova *et al*., 2008), but a short review is informative. As one influential example, Ashley Montagu (1940) conjectured that tooth agenesis resulted from inadequate space in the developing maxillary dental arch. Montagu was focusing specifically on the maxillary lateral incisor that forms on the lateral border of the premaxilla next to the maxillary-premaxillary suture (Behrents and Harris, 1991). Ashley Montagu's contention—which was well reasoned but unsupported by any test—was that tooth size responds to the available space of the supporting bone. Ashley Montagu speculated that, across eons—as what is now the orthognathic human face diminished in size from prognathic predecessors—tooth sizes (and, especially, size of the maxillary lateral incisors) diminished coincident with increases in pegging and congenital absence of various tooth types. As regards the maxillary lateral incisor that is quite variable (at least in European peoples; Harris and Rathbun, 1991), Ashley Montagu concluded that this dental variability is due to the phylogenetic reduction of the premaxilla.

Ashley Montagu sidesteps the question why the canine, the other tooth adjacent to the maxillary-premaxillary suture, is, in contrast, one of the most stable tooth types. He also avoids the problem (except in his introduction) of why the mandibular incisors are not comparably variable, though sizes of the two jaws have necessarily been reduced to similar extents. Ashley Montagu's scenario—that reduced bony support leads to reduced tooth sizes—also seems at odds with the third molar located at the distal terminus of the arches also being quite variable even though these molars occur at the other end of the dental ach and form much later than the incisors (Haavikko, 1970). It seems that different agents are responsible within each tooth type.

Sofaer (*e.g*., 1969, 1979) seems to promote this same idea of inadequate formative space as a general explanation for hypodontia, though this is unsubstantiated by our current understanding of tooth morphogenesis. This conjecture also ignores the three-dimensional dispersions of the developing tooth

Correspondence to: Edward Harris, Department of Orthodontics, 870 Union Avenue, University of Tennessee, Memphis, Tennessee 38163.
E-mail: eharris@utmem.edu

germs. While it is a graphic metaphor to suppose that a formative tooth bud might be "choked" out of existence due to inadequate bony support, there are no data to support this. Instead, cytokines from the dental follicle attract osteoclasts during normal development (Marks and Cahill, 1983), and these clast cells progressively enlarge the surrounding tooth crypt to accommodate the developing tooth (Carlson, 1944). This is readily seen (and palpatable) in infants, where the buccolingual diameters of the primary tooth crypts have enlarged well beyond the incipient bony ridges, and the surfaces of the ridges are scalloped due to these out-pouchings (*e.g.*, van der Linden and Duterloo 1976). The emergence of teeth into a tight-fitting arcade of teeth as seen in the adult is not indicative of the three-dimensional arrangement of tooth crypts—plus the temporal span during which different teeth form. For example, the canine abuts against the lateral incisor in the adult, but (A) the lateral incisor forms much earlier, when there is plenty of room in the supporting jaws, and (B) when the canines do form, their positions are far apical of the other teeth.

Molecular biology now makes it clear that a tooth will fail to develop if there is no ectodermal signal to stimulate a site along the underlying mesenchyme to initiate tooth formation (Kollar and Baird, 1970a,b). This cause of hypodontia seems primarily genetic in nature, but failure of formation also can be affected by the environment. Suggestions from animal studies are that tooth buds that fail to reach a critical size will resorb—resulting in hypodontia rather than continuing to develop. Likewise, environmental stressors acting at the critical early stages of formation can simply kill off a tooth bud. Teratogenic drug actions and irradiation are well-studied examples of this (Bruce, 1950; Kaste *et al.*, 1998). Yet a third mechanism involves a genetic interruption of the cascade of molecular signals leading to tooth formation. This is obvious in the edentates (*e.g.*, armadillos, anteaters; Todd, 1918) where there is initial tooth formation, but development ceases early in the bell stage. This interruption also accounts for the "missing teeth" (absence of lateral incisors, canines, and premolars) that is characteristic of mice and other rodents. (See review by Peterkova *et al*. 2006.) The extreme example of this inhibition of tooth development probably is in birds (the class Aves), where all modern birds are tooth-less but tooth formation can be reintroduced experimentally (Chen *et al*., 2000; Mitsiadis *et al.*, 2006). At an allelic level, it is conceivable that this sort of interruption of molecular events accounts for the variable frequencies of tooth agenesis in humans (*e.g.*, Matalova *et al*., 2008).

Numerous clinical and physical anthropological studies have reported on the frequencies of missing M3s in humans. The purpose of the present study is to investigate the pattern of missing M3s in some detail within and among individuals in population samples. That is, there are 4 M3s distributed as left-right pairs in the two dental arches, and the issue is how hypodontia is distributed among these 4 sites. This study is restricted to M3s, though there are evident associations among tooth types (Davies, 1968; Khalaf *et al*., 2005; Harris and Clark, 2008). As pertinent examples, Alvesalo and Portin (1969) and Woolf (1971), among others, have documented that the maxillary lateral incisor is more often affected (diminished size, pegged, absent) in individuals with hypodontic M3s versus those with developmentally intact dentitions; hypodontia is not an isolated phenomenon, even among tooth types that form at quite different ages.

MATERIALS AND METHODS

Panoramic radiographs (van der Linden and Duterloo, 1976) of 1,700 adolescents were studied. Most (1,100) were American whites, and the rest were American blacks (600), all from clinical records at the College of Dentistry, University of Tennessee, Memphis. Subjects were selected with radiographs taken between 12 and 18 years of age. These adolescents were old enough that their M3s would have begun mineralization if they were going to form (Rantanen, 1967; Harris, 2007), but the adolescents were young enough to well remember having any M3s extracted. It seems obvious that hypodontia has to be documented radiographically, especially for M3s that commonly form but do not erupt into the oral cavity. Sample sizes vary among the statistical tests described here because not every tooth's existence could be documented because of radiographic issues.

One intent was to estimate the background frequencies of M3 hypodontia in these two ethnic groups, so subjects with a recognized craniofacial syndrome, including facial clefts, were omitted since they have characteristic—often elevated—patterns of hypodontia (*e.g.*, Schalk-van der Weide, 1992; Ranta, 1983; Harris and Hullings, 1990).

Tooth formation can be viewed as a dichotomous event—a tooth has either developed or it is absent. With potentially one M3 in each quadrant, there are 16 permutations of hypodontia. Expansion of the binomial shows that there are five M3 groupings, namely (A) all 4 M3s present, (B) four arrangements with 1 tooth missing, (C) 6 arrangements with just 2 teeth missing, (D) 4 arrangements of 3 teeth missing, and (E) one situation where all 4 M3s are hypodontic. In other words, the 16 permutations are arranged in the familiar ratios of 1:4:6:4:1.

Statistical tests relied on chi-square analysis. Statistics were performed using JMP 7.0 (SAS, Cary, NC). The kappa statistic was calculated as the measure of association (Fisher and van Belle, 1993).

RESULTS

The observed frequency of M3 hypodontia for the total sample (Table 1) shows that the distribution is far from random. Despite common perceptions that hypodontia of M3 is common, most people experience development of all 4 M3s (86.8%; 1449/1670), whereas congenital absence of all 4 M3s occurred in just 1.6% of the cases. Fig. 1 shows that the distribution of severity (*i.e.*, number of congenitally absent M3s) approximates the right-end of a normal distribution, where the frequency decreases as the number of missing M3s increases. The perception that M3s frequently are absent is strongly influenced by the widespread prophylactic extraction of M3s in the late teens (*e.g.*, Eklund and Pittman, 2001).

Black-White differences

American blacks and whites have been admixing for centuries, though admixture estimates are lower in the Southeast than elsewhere in the nation because of harsher social and legal proscriptions (Williamson, 1980; Davis, 1991). Blacks have larger and morphologically more complex teeth (Richardson and Malhotra, 1975; Irish, 1997), and, evidently in an associated manner, discernibly lower frequencies of hypodontia (Harris and Clark, 2008). Stanley Garn contended in several of his publications (notably 1977) that tooth size, morphology, tempo of formation, and occurrence (in contrast to congenital absence) are positively intercorrelated features of a common underlying theme in tooth formation, not isolated phenomena—and that these features differ among tooth types controlled, at a primary level, by a tooth's position in its morphogenetic field.

Table 2 shows the distributions in each of the arches (sexes pooled). In both jaws, whites have highly significantly higher frequencies of M3 hypodontia, and the source of the significance is primarily due to deficits of bilateral absence in blacks compared to whites (as assessed from the cell chi squares).

Little is known about hypodontia in other, non-Caucasian races; most work has been done on peoples of European extraction where frequencies and the patterning of hypodontia among tooth types probably is not representative of all groups. Röse (1906) and Hrdlička (1921) each collated data from large series of peoples of diverse races—but with ill-defined criteria and without the benefit of radiography to confirm congenital absence. Still, differences in the frequencies of hypodontia are evident in these early studies. Population differences in trait frequencies are prima facie evidence for a genetic influence on the risk of hypodontia.

Sexual dimorphism

The data in Table 1 were dichotomized into cases

TABLE 1. Distributions of M3 congenital absence by race and sex

Number Missing	Whites						Blacks						Total Sample	
	Males		Females		M+F		Males		Females		M+F			
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
0	396	86.09	504	80.77	900	83.03	254	95.13	294	92.45	548	93.68	1448	86.76
1	25	5.43	49	7.85	74	6.83	8	3.00	11	3.46	19	3.25	93	5.57
2	29	6.30	41	6.57	70	6.46	3	1.12	10	3.14	13	2.22	83	4.97
3	5	1.09	12	1.92	17	1.57	1	0.37	0	0.00	1	0.17	18	1.08
4	5	1.09	18	2.88	23	2.12	1	0.37	3	0.94	4	0.68	27	1.62
Sums	460		624		1,084		267		318		585		1,669	

TABLE 2. Frequencies of M3 hypodontia in American Blacks and Whites

	Whites			Blacks				
Statistic	Both Absent	One Absent	Both Present	Both Absent	One Absent	Both Present	df	Chi-square[1]
				Maxilla				
%	5.0	4.0	90.9	1.7	3.2	95.1		
n	56	45	1010	10	19	561	2	12.6
				Mandible				
%	4.5	3.1	92.5	1.2	1.5	97.3		
n	74	51	1534	7	9	572	2	17.8

[1]Both X^2 values are highly significant ($P < 0.0001$) because M3 hypodontia is more common in whites than blacks.

without M3 hypodontia and cases missing one or more M3s. This showed that hypodontia is significantly more common in girls than boys in whites ($\chi^2 = 5.3$; df =1; P = 0.02). The source of significance (based on cell chi squares) is primarily due to the comparative deficit of hypodontia in males. 14% of males exhibit agenesis of one or more M3s, compared to 19% of females. The overall frequency is appreciably lower in American blacks (*ca.* 6% *vs*. about 16% in whites) and, with the smaller sample size of 600, the sex difference is not significant here ($\chi^2 = 1.8$; df = 1; P = 0.1850). If the present frequencies hold, a sample size roughly three times larger (*ca*. 2,000) would be needed to achieve statistical significance in blacks.

In addition to the greater frequencies of M3 hypodontia in females, Fig. 2 shows that severity—as measured by the number of missing M3s—also is greater in females than males. This shift towards greater expression in females is more obvious in whites because of their greater incidence of M3 hypodontia overall.

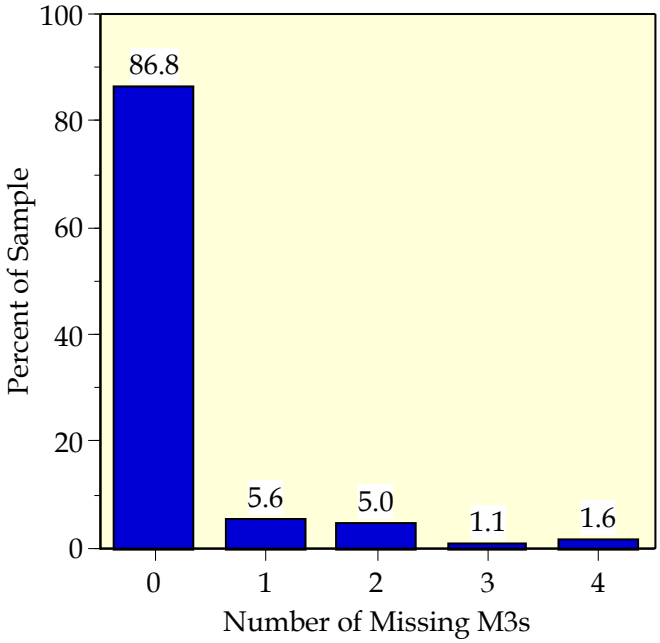

Fig. 1. Percentage distribution of M3 hypodontia in the total sample.

Arcade effects

There are positive, statistically significant associations for M3 hypodontia between all four M3s taken pairwise; the matrix of kappa correlations (Table 3) based on the total sample shows that left-right symmetry is highest (kappa ~ 0.7) within each arch, and the inter-arch associations are appreciably lower (kappa ~ 0.3), but correlations within and between hemispheres seem equivalent. Hierarchically, the symmetry between sides is much higher than between arches, but whether the association between the arches is taken between the same or opposite quadrants seems immaterial.

A related point is that asymmetric occurrence is relatively uncommon. M3 status in one quadrant strongly predicts the same status in the antimeric site. This is anticipated since our understanding is that the same genotype affects tooth development in the left and right quadrants, with effectively the same environment in each to achieve a tooth's phenotype. Dental researchers have sought evidence for laterality or sidedness, primarily using data on crown dimensions. Documentations of laterality are few and scattered among samples (*e.g.*, Harris, 1992; Townsend *et al*., 1999). The bulk of left-right asymmetry is expressed as random (fluctuating) asymmetry, at least with regard to size.

Figure 3 arborizes the frequencies of hypodontia by tooth type and, thereby, shows the dependencies (statistical associations) between the arches. An obvious "dose-dependent" relationship from among several of the associations is this: When both upper molars are congenitally absent, just 50% of the two mandibular molar molars are present. When just one upper molar is present, the frequency of the two lower molars being

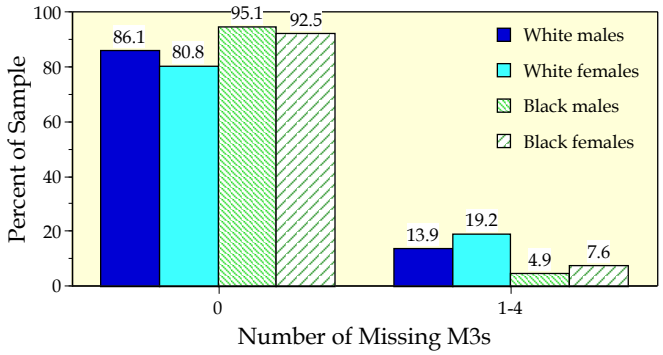

Fig. 2. The frequencies of the congenital absence of M3 (all expressivities combined) by race and sex. M3 hypodontia is more common in American whites than blacks, and more frequent in girls than boys in each race, though the extent of sexual dimorphism is appreciably higher in whites, perhaps because the overall incidence is higher in whites.

absent rises to 70%. And, when neither upper M3 is absent, the frequency of both lower molars being agenetic rises to a high of 94%.

Side effects

Sidedness is the interesting situation where there is preferential laterality: Does absence of a tooth on one side influence absence of the same tooth in the opposing arch? The informative cases are those where either the left or right molar is absent in the maxilla and likewise (unilateral absence) in the mandible. Unfortunately, cases of unilateral congenital absence in both dental arches are uncommon, just 7 cases in the 1,670 individuals where all 4 M3s could be scored. These 7 cases were equally distributed (3:4) as to arrangements where the ipsilateral tooth (same hemisphere) was missing in the two arches versus where the contralateral tooth (opposite hemisphere) was absent. At least with these few informative cases, there is no suggestion of sidedness.

Another way of viewing laterality is simply whether M3 is more common on one side of the mouth than the other. The maxillary left-right distribution of unilateral presence is 33 (left only) compared to 32 (right only), which is indistinguishable statistically from a random spread of 50:50. In the mandible, the left-right distribution of congenital absence is 27 (left only) compared to 34 (right only). This does not depart from a 50:50 chance occurrence (P = 0.53). Congenital absence of M3 is, then, equally distributed between sides.

DISCUSSION

Hypodontia in itself suggests a phenotypic dichotomy: the tooth either is present or absent. Features of hypodontia, notably the increased frequencies among relatives of affected individuals (Grahnén, 1956; Brook, 1984), imply a hereditary basis for the condition, though the mode of transmission is not simple (Mendelian). Differences in population frequencies among inbred strains of laboratory animals (*e.g.*, Grüneberg, 1952; Chai and Chiang, 1962; Sofaer, 1969) and among human groups (*e.g.*, Ashley Montagu, 1940; Polder *et al.*, 2002; Harris and Clark, 2008) likewise favors some genetic basis for hypodontia. Sex differences in rates of occurrence (typically with the frequency and severity of agenesis being greater in females) is a third indicator that genes influence a person's risk (Egermark-Eriksson and Lind, 1971). The dramatic effects of some major genes, notably the suite of genes causing forms of HED (hypohidrotic ectodermal dysplasia), might also be mentioned here, but these phenotypes are characterized by oligodontia or, even, anodontia, so they do not stem from the same alleles leading to the absence of a single or just a very few teeth as occurs in most people with hypodontia (Schalk-van der Weide, 1992).

Elucidation over the past few years of specific molecular signaling factors that predispose for hypodontia, such as Pax 9, Msx 1, Msx 2, and others, greatly strengthens the argument for a genetic basis of congenital absence (*e.g.*, Mostowska *et al.*, 2003; Viera, 2004; Larmour *et al.*, 2005). These few first molecular factors to be identified are, predictably, those with clear-cut effects on the phenotypes—where affected individuals commonly are missing multiple teeth. Analytical refinements (and larger sets of family data) will lead to documentation of genes with subtler but probably more common frequencies in the general population. Work to date shows that deleterious alleles (Pax 9 and so forth) enhance the risk of hypodontia, but they do not fully determine it, and the variable expressivity among cases likely is due to (A) the individual's genetic background against which these alleles are expressed and (B) environmental conditions that modulate expression.

Quasicontinuous model

Hypodontia as expressed in most humans (with one or a few missing dental elements) has no known etiology. It is, however, common enough to warrant the attention of many dental researchers. A popular model of inheritance that accounts for the observed phenotypic distributions of the condition is quasicontinuous inheritance. The supposition is that some indefinite number of genes collectively contribute to trait expression (where "expression" here is congenital absence). This is the common polygenic model (*e.g.*, Falconer, 1989), but with a threshold (Fig. 4). The threshold is toward the lower end of the supposed underlying genotypic array. For the bulk of the population (that is above the threshold) teeth are present. It is in those comparatively few cases who

TABLE 3. Correlation coefficients (kappa) between the four third molars taken pairwise[1]

	Upper Left	Upper Right	Lower Left
Upper Right	0.66 (0.0400)		
Lower Left	0.31 (0.0437)	0.33 (0.0439)	
Lower Right	0.30 (0.0442)	0.31 (0.0444)	0.71 (0.0356)

[1]Values in parentheses are the standards errors of the estimates; all 6 correlations are highly significantly different from zero ($P < 0.0001$).

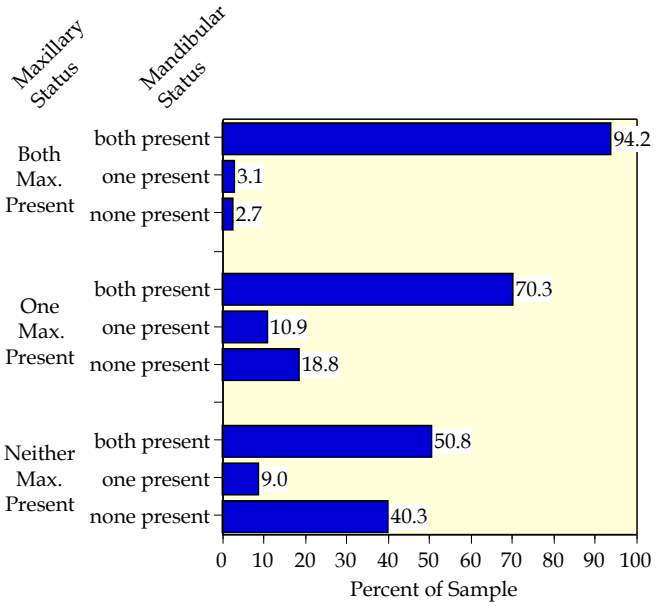

Fig. 3. Dependence between arches in the occurrence of M3s. (***Top***) When both maxillary M3s are present, 94% of cases have both mandibular M3s present. (***Middle***) when just one of the two maxillary molars is present, the frequency of both lower M3s being present drops to 70%. (***Bottom***) When both maxillary M3s are congenitally absent, the frequency of both lower M3s being present is just 40%. These associations indicate nothing about cause and effect; the same dependencies are found if the lower molars are taken as the predictive variable.

are below the threshold that hypodontia occurs.

There is an interesting but tangled history of this model. Many physical anthropologists, particularly those with interests in skeletal biology, attribute it to the work of Hans Grüneberg (1950, 1952) who marshaled the quasicontinuous model (QCM) as an explanation for the numerous minor skeletal variants he studied in mice, such as accessory foramina, ossicles, and other morphological features, that occur in some animals but not others. The utility of these "discrete" (*i.e.*, present or absent) skeletal features for phenetic studies of human skeletal series was popularized by A. C. Berry and R. J. Berry (*e.g.*, 1967, 1968, 1974).

Grüneberg's work in turn rested on the seminal studies of Sewall Wright in the 1930s. Wright (1934a,b) explored the inheritance of the number of digits on the hind feet of guinea pigs, which normally have 3 digits but may have 4, and attributed the occurrence of 4 toes to the guinea pig's genotype exceeding what he termed a "physiological threshold." Indeed, his Figure 1 (1934b, p. 544) depicts the presumed underlying polygenic model as a normal curve overlying two successive thresholds, a lower one, where poorly-formed ("vestigial") 4th toes occur, and a higher one, where the 4th toe is eumorphic. This development of a two-threshold scheme is precisely what was exploited later by Reich and others (Reich *et al.*, 1972; Corbett *et al.*, 2004) to provide practical statistical tests for distinguishing between single-gene and polygenic models of inheritance. While Wright did not formalize the QCM, he described its major features during his various breeding experiments. Denys Falconer (1965) elaborated the assumptions and statistical expectations of the QCM. Falconer described how heritability ($V_{additive}$ / V_{total}) of a trait could be estimated from trait frequencies. However, this requires family data (information on relatives of known degrees of biological relatedness). Heritability cannot be calculated from samples of cases without known relationships, so this useful aspect of the QCM generally has been ignored in skeletal biological studies, but with some noteworthy exceptions: Saunders and Popovich (1978) recorded minor skeletal variants from radiographs of siblings enrolled in the Burlington Growth Study. Sjøvold (1984, 1996) analyzed skulls of Europeans where genealogical information had been preserved. Cheverud and colleagues (*e.g.*, McGrath *et al.*, 1984; Richtsmeier *et al.*, 1984) used the unique setting of the island of Cayo Santiago (where genealogical affinities of most monkeys is known) to estimate heritability of several nonmetric bony features in macaques.

The work of Carter (notably 1969) warrants mention here because (A) he demonstrated the applicability of a threshold model for many common diseases (*e.g.*, pyloric stenosis, diabetes mellitus, spina bifida cystica, and others), which did much to familiarize the health care community with this quasicontinuous model and

(B) he listed several criteria that, when met, can be very suggestive of a polygenic threshold model.

While largely beyond the scope of this paper, it is informative to note that James (1971) pointed out that too many parameters need to be estimated than can be obtained from a QCM with one threshold. But, adequate parameters are available if two thresholds are supposed in the model, and James worked with Ted Reich (*e.g.*, Reich *et al.* 1972; Corbett *et al.* 2004) to develop tests that can distinguish between inheritance due to a single-gene model versus a polygenic model. Suarez and Spence (1974) applied a basic form of this approach to the hypodontia family data collected by Grahnén (1956), concluding that a polygenic threshold model fit the data appreciably better than expectations of the effects of single gene.

QCM and Hypodontia

Davies (1968), Sofaer (1969), Bailit (1975), and Chosack *et al.* (1975), among others, alluded to the QCM fitting observations seen in population samples, but Brook (1984) was the first to seriously develop the QCM to hypodontia (and, at the other, complementary extreme, hyperdontia). Brook emphasized the developmental interrelationships between hypodontia and tooth size. There also is a well-documented relationship between hypodontia and crown sizes of the remaining teeth; people in the population who do not have hypodontia have statistically larger teeth than those with congenital absence (Garn and Lewis, 1962; Garn *et al.*, 1962, 1963, 1970). Conversely, diminished crown sizes and microdontia are more common in those with hypodontia than in those with full complements of teeth. These clinical results are duplicated in laboratory animals (Grüneberg, 1950, 1952; Self and Leamy, 1978). The greater the extent of hypodontia, the greater the size reductions and the greater likelihood of microdontia (with associated missing cusps and simplified morphologies of the remaining teeth). Numerous studies of European groups have found higher frequencies of hypodontia in females than males (reviewed in Egermark-Eriksson and Lind, 1971). These several associations suggest that hypodontia has dentition-wide systemic effects, which is predictable since teeth form as repetitive elements (a meristic series; Bateson, 1894) using the same regulatory mechanisms controlled by the person's genotype (Kettunen and Thesleff, 1998; Jernvall and Thesleff, 2000).

Grüneburg (1952) documented differences in the frequencies of third molar hypodontia among inbred strains of mice. Mice with larger teeth had lower frequencies of M3 hypodontia than strains with smaller teeth. The same relationship is evident in humans, where African Americans (with large teeth) exhibit M3 hypodontia infrequently compared to American whites with smaller crown sizes and higher frequencies (and greater severities) of M3 hypodontia (Harris and Clark, 2008). Hyperdontia (supernumerary teeth) is, in contrast, more common in males (*e.g.*, Stafne, 1932; Khalaf *et al.*, 2004).

This collage of interrelated features recently has been extended by Uslenghi *et al.* (2006) who showed that hypodontia is associated with slowed tooth development (also see Garn *et al.* 1961).

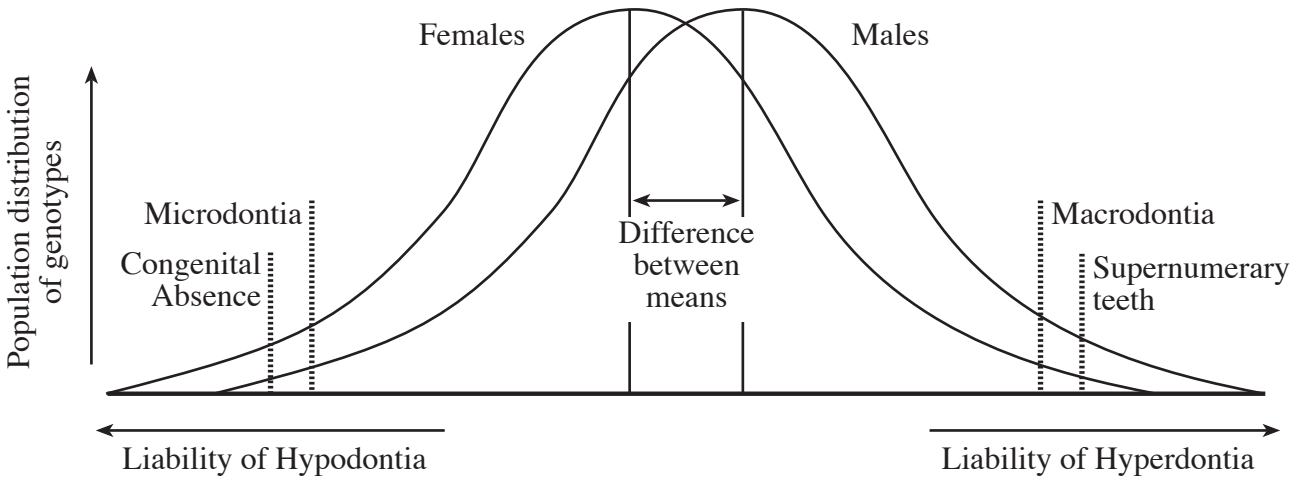

Fig. 4. Schematic of the quasicontinuous model (modified from Brook, 1984). There is an underlying genotypic range in a population that influences a person's risk for hypodontia (left extreme) and hyperdontia (right extreme). Sex-specific distributions are shown here to reflect the greater risk of congenital absence in women versus the greater risk of supernumerary teeth in men—at least in peoples of European extraction. Sexual dimorphism appears to be lower in peoples of subSaharan extraction. The vertical bars are depicted as broken lines since a person's genotype can be modulated in either direction by the environment.

OVERVIEW

The present study assessed the phenotypic patterns of third molars (M3) congenital absence in 1,700 teenagers composing a contemporary cohort of American blacks and whites from the Southeast United States.

- There is no difference by arcade, but agenic M3s are significantly more common in females than males and in American whites compared to American blacks.
- No evidence of sidedness (preferential absence on one side) could be discerned, and asymmetry (unilateral occurrence) is fairly uncommon versus symmetric presence or absence.
- Congenital absence of one M3 is highly predictive of other missing M3s, suggesting common developmental associations that probably are modulated by the person's genetic background.
- While genes with rather severe effects on congenital absence have been documented, most cases of hypodontia are of unknown etiology, although population distributions are in concert with a quasicontinuous model of inheritance (also termed a polygenic threshold model).

LITERATURE CITED

Alvesalo L, Portin P. 1969. The inheritance pattern of missing, peg-shaped, and strongly mesio-distally reduced upper lateral incisors. Acta Odontol Scand 27:563-575.

Ashley Montagu MF. 1940. The significance of the variability of the upper lateral incisor teeth in man. Hum Biol 12:323-358.

Bailit HL. 1975. Dental variation among populations: an anthropologic view. Dent Clin No Am 19:125-140.

Bateson W. 1894. Materials for the study of variation: treated with special regard to discontinuity in the origin of species. London: Methuen.

Behrents RG, Harris EF. 1991. The premaxillary-maxillary suture and orthodontic mechanotherapy. Am J Orthod Dentofacial Orthop 99:1-6.

Berry AC. 1974. The use of non-metrical variations of the cranium in the study of Scandinavian population movements. Am J Phys Anthropol 40:345-358.

Berry AC, Berry RJ. 1967. Epigenetic variation in the human cranium. J Anat 101:361-379.

Berry RJ. 1968. The biology of non-metrical variation in mice and men. In: Brothwell DR, editor. The skeletal biology of earlier human populations. London: Pergamon Press, p 103-133.

Brook AH. 1984. A unifying aetiological explanation for anomalies of human tooth number and size. Arch Oral Biol 29:373-378.

Bruce KW. 1950. The effect of irradiation on the developing dental system of the Syrian hamster. Oral Surg 3:1468-1477.

Carlson H. 1944. Studies on the rate and amount of eruption of certain human teeth. Am J Orthod Oral Surg 30:575-588.

Carter CO. 1969. Genetics of common disorders. Br Med Bull 25:52-57.

Chai CK, Chiang MSM. 1962. The inheritance of careener, unbalanced locomotion in mice. Genetics 47:435-441.

Chen Y, Zhang Y, Jiang TX, Barlow AJ, St Amand TR, Hu Y, Heaney S, Francis-West P, Chuong CM, Maas R. 2000. Conservation of early odontogenic signaling pathways in Aves. Proc Natl Acad Sci U S A 97:10044-10049.

Chosack A, Eidelman E, Cohen T. 1975. Hypodontia: a polygenic trait—a family study among Israeli Jews. J Dent Res 54:16-19.

Corbett J, Gu CC, Rice JP, Reich T, Province MA, Rao DC. 2004. Power loss for linkage analysis due to the dichotomization of trichotomous phenotypes. Hum Hered 57:21-27.

Davies PL. 1968. Agenesis of teeth of the permanent dentition: a frequency study in Sydney schoolchildren. Aust Dent J 13:146-150.

Davis FJ. 1991. Who is Black? One nation's definition. University Park: Pennsylvania State University Press.

Egermark-Eriksson I, Lind V. 1971. Congenital numerical variation in the permanent dentition. D. Sex distribution of hypodontia and hyperodontia. Odontol Revy 22:309-315.

Eidelman E, Chosack A, Rosenzweig KA. 1973. Hypodontia: prevalence amongst Jewish populations of different origin. Am J Phys Anthropol 39:129-133.

Eklund SA, Pittman JL. 2001. Third-molar removal patterns in an insured population. J Am Dent Assoc 132:469-475.

Falconer DS. 1965. The inheritance of liability to certain diseases, estimated from the incidence among relatives. Ann Hum Genet 29:51-71.

Falconer DS. 1989. Introduction to quantitative genetics, 3rd ed. New York: John Wiley & Sons.

Fisher LD, van Belle G. 1993. Biostatistics: a methodology for the health sciences. New York: John Wiley and Sons, Inc.

Garn SM. 1977. Genetics of tooth development. In: McNamara JA, editor. The biology of occlusal development (Craniofacial growth series). Ann Arbor, MI: Center for Human Growth and Development, University of Michigan. p 61–88.

Garn SM, Lewis AB. 1962. Relationship between third molar agenesis and reduction in tooth number. Angle Orthod 32:14-18.

Garn SM, Lewis AB. 1970. The gradient and the pattern of crown-size reduction in simple hypodontia. Angle Orthod 40:51-58.

Garn SM, Lewis AB, Bonné B. 1961. Third molar polymorphism and the timing of tooth formation.

Nature 192:989.
Garn SM, Lewis AB, Vicinus JH. 1962. Third molar agenesis and reduction in number of other teeth. J Dent Res 41:717.
Garn SM, Lewis AB, Kerewsky RS. 1963. Third molar agenesis and size reduction of the remaining teeth. Nature 230:488-489.
Grahnén H. 1956. Hypodontia in the permanent dentition: a clinical and genetical study. Odont Revy 7:suppl 3.
Grüneberg H. 1950. Genetical studies on the skeleton of the mouse. I. Minor variations of the vertebral column. J Genet 50:112-141.
Grüneberg H. 1952. Genetical studies on the skeleton of the mouse. IV. Quasi-continuous variations. J Genetic 51:95-114.
Haavikko K. 1970. The formation and the alveolar and clinical eruption of the permanent teeth: an orthopantomographic study. Proc Finn Dent Soc 66:103-170.
Harris EF. 1992. Laterality in human odontometrics: Analysis of a contemporary American White series. In: Lukacs JR, editor. Culture, ecology and dental anthropology. Chawri-Bazar, Delhi: Kamla-Raj Enterprises, p 157-170.
Harris EF. 2007. Mineralization of the mandibular third molar: a study of American blacks and whites. Am J Phys Anthropol 132:98-109.
Harris EF, Clark LL. 2008. Hypodontia: an epidemiological study of American blacks and whites. Am J Orthod Dentofacial Orthop 134:761-767.
Harris EF, Hullings JG. 1990. Delayed dental development in children with isolated cleft lip and palate. Arch Oral Biol 35:469-473.
Harris EF, Rathbun TA. 1991. Ethnic differences in the apportionment of tooth sizes. In: Kelley MA, Larsen CS, editors. Advances in dental anthropology. New York: Alan R. Liss, Inc., p 121-142.
Hrdlička A. 1921. Further studies on tooth morphology. Am J Phys Anthropol 4:141-176.
Irish JD. 1997. Characteristic high- and low-frequency dental traits in sub-Saharan African populations. Am J Phys Anthropol 102:455-467.
James JW. 1971. Frequency in relatives for an all-or-none trait.Ann Hum Genet 35:47-49.
Jernvall J, Thesleff I. 2000. Reiterative signaling and patterning during mammalian tooth morphogenesis. Mech Dev 92:19-29.
Kaste SC, Hopkins KP, Bowman LC, Santana VM. 1998. Dental abnormalities in children treated for neuroblastoma. Med Ped Oncol 30:22-27.
Kettunen P, Thesleff I. 1998. Expression and function of FGFs-4, -8, and -9 suggest functional redundancy and repetitive use as epithelial signals during tooth morphogenesis. Dev Dyn 211:256-268.
Khalaf K, Robinson DL, Elcock C, Smith RN, Brook AH. 2005. Tooth size in patients with supernumerary teeth and a control group measured by image analysis system. Arch Oral Biol 50:243-248.
Kirkham J, Kaur R, Stillman EC, Blackwell PG, Elcock C, Brook AH. 2005. The patterning of hypodontia in a group of young adults in Sheffield, UK. Arch Oral Biol 50:287-291.
Kollar EJ, Baird GR. 1970a. Tissue interactions in embryonic mouse tooth germs. I. Reorganization of the dental epithelium during tooth-germ reconstruction. J Embryol Exp Morphol 24:159-171.
Kollar EJ, Baird GR. 1970b. Tissue interactions in embryonic mouse tooth germs. II. The inductive role of the dental papilla. J Embryol Exp Morphol 24:173-186.
Larmour CJ, Mossey PA, Thind BS, Forgie AH, Stirrups DR. 2005. Hypodontia—a retrospective review of prevalence and etiology. Part I. Quintessence Int 36:263-270.
Marks SC Jr, Cahill DR, Wise GE. 1983. The cytology of the dental follicle and adjacent alveolar bone during tooth eruption in the dog. Am J Anat 168:277–289.
Mattheeuws N, Dermaut L, Martens G. 2004. Has hypodontia increased in Caucasians during the 20th century? A meta-analysis. Eur J Orthod 26:99-103.
Matalova E, Fleischmannova J, Sharpe PT, Tucker AS. 2008. Tooth agenesis: from molecular genetics to molecular dentistry. J Dent Res 87:617-623.
McGrath JW, Cheverud JM, Buikstra JE. 1984. Genetic correlations between sides and heritability of asymmetry for nonmetric traits in rhesus macaques on Cayo Santiago. Am J Phys Anthropol 64:401-411.
Mitsiadis TA, Caton J, Cobourne M. 2006. Waking-up the sleeping beauty: recovery of the ancestral bird odontogenic program. J Exp Zoolog B Mol Dev Evol 306:227-233.
Mostowska A, Kobielak A, Trzeciak WH. 2003. Molecular basis of non-syndromic tooth agenesis: mutations of MSX1 and PAX9 reflect their role in patterning human dentition. Eur J Oral Sci 111:365-370.
Nanda RS. 1954. Agenesis of the third molar in man. Am J Orthod 40:698-706.
Peterkova R, Lesot H, Peterka M. 2006. Phylogenetic memory of developing mammalian dentition. J Exp Zoolog B Mol Dev Evol 306:234-250.
Pindborg JJ. 1970. Pathology of the dental hard tissues. San Francisco: WB Saunders Company.
Polder BJ, Van't Hof MA, Van der Linden FP, Kuijpers-Jagtman AM. 2004. A meta-analysis of the prevalence of dental agenesis of permanent teeth. Community Dent Oral Epidemiol 32:217-226.
Ranta R. 1983. Hypodontia and delayed development of the second premolars in cleft palate children. Eur J Orthod 5:145-148.
Rantanen AV. 1967. The age of eruption of the third molar teeth. Acta Odont Scand 25:1-86.

Reid DJ, Dean MC. 2006. Variation in modern human enamel formation times. J Hum Evol 50:329-346.

Richardson ER, Malhotra SK. 1975. Mesiodistal crown dimension of the permanent dentition of American Negroes. Am J Orthod 68:157-164.

Reich T, James JW, Morris CA. 1972. The use of multiple thresholds in determining the mode of transmission of semi-continuous traits. Ann Hum Genet 36:163-184.

Richtsmeier JT, Cheverud JM, Buikstra JE. 1984. The relationship between cranial metric and nonmetric traits in the rhesus macaques from Cayo Santiago. Am J Phys Anthropol 64:213-222.

Röse C. 1906. Ueber die Rückbildung der seitlichen Schneiderzähne des Oberkiefers und der Weisheitszähne im menschlichen Gebisse. D Monat f Zahnheil 24:225-258.

Saunders SR, Popovich F. 1978. A family study of two skeletal variants: atlas bridging and clinoid bridging. Am J Phys Anthropol 49:193-203.

Schalk-van der Weide Y. 1992. Oligodontia: a clinical, radiographic and genetic evaluation. Utrecht: Rijksuniversiteit Utrecht.

Self SG, Leamy L. 1978. Heritability of quasi-continuous skeletal traits in a randombred population of house mice. Genetics 88:109-120.

Sjøvold T. 1984. A report on the heritability of some cranial measurements and non-metric traits. In: Van Vark GN, Howells WW, editors. Multivariate statistical methods in physical anthropology. Boston: D. Reidel Publishing Company, p 223-246.

Sjøvold T. 1996. Testing assumptions for skeletal studies by means of identified skulls from Hallstatt, Austria. In: Saunders SR, Herring A, editors. Grave reflections: portraying the past through cemetery studies. Toronto: Canadian Scholars' Press Inc, p 241-281.

Sofaer JA. 1969. The genetics and expression of a dental morphological variant in the mouse. Arch Oral Biol 14:1213-1223.

Sofaer JA. 1979. Human tooth-size asymmetry in cleft lip with or without cleft palate. Arch Oral Biol 24:141-146.

Stafne EC. 1932. Supernumerary teeth. Dent Cosmos 74:653-659.

Suarez BK, Spence MA. 1974. The genetics of hypodontia. J Dent Res 53:781-785.

Thompson GW, Popovich F, Anderson DL. 1974. Third molar agenesis in the Burlington Growth Centre in Toronto. Community Dent Oral Epidemiol 2:187-192.

Todd TW. 1918. An introduction to the mammalian dentition. St. Louis: C. V. Mosby Company.

Townsend G, Dempsey P, Richards L. 1999. Asymmetry in the deciduous dentition: fluctuating and directional components. Perspect Hum Biol 4:45-52.

Uslenghi S, Liversidge HM, Wong FS. 2006. A radiographic study of tooth development in hypodontia. Arch Oral Biol 51:129-133.

van der Linden FPGM, Duterloo HS. 1976. Development of the human dentition. Hagerstown, PA: Harper and Rowe Publishers.

Vieira AR. 2003. Oral clefts and syndromic forms of tooth agenesis as models for genetics of isolated tooth agenesis. J Dent Res 82:162-165.

Williamson J. 1980. New people: miscegenation in the United States. New York: The Free Press.

Woolf CM. 1971. Missing maxillary lateral incisors: a genetic study. Am J Hum Genet 23:289-296.

Wright S. 1934a. An analysis of variability in number of digits in an inbred strain of guinea pigs. Genetics 19:506-536.

Wright S. 1934b. The results of cross between inbred strains of guinea pigs differing in number of digits. Genetics 19:537-551.

Joined supernumerary mandibular teeth in the premolar region: Report of a Hungarian archeological case

Gy. Szabó*, G. Kocsis S., E. Molnár

University of Szeged, Department of Anthropology, Szeged – Hungary, H-6701

ABSTRACT Supernumerary teeth are those that are additional to the normal complement. They may occur in any region of the dental arch and have been reported in both the primary and the permanent dentitions. The etiology of supernumerary teeth is still not clearly understood, but several theories have been suggested for their occurrence. The investigated material were the remains from the Bácsalmás-Óalmás burial site (from the 16th-17th centuries), where 472 skeletons were excavated from 1993 to 2003. For the purpose of this study, the dentitions of 164 adult individuals were examined. The examination was carried out using macromorphological methods, radiographic analysis and a dial caliper were applied. This paper describes a supernumerary tooth of an adult female skeleton. On the labial surface of the first mandibular premolar an extra tooth was observed. Radiographic examination of the fused teeth indicated that the crown of the premolar had fused incompletely with the crown of the extra tooth. The position of the extra tooth could have been the result of gemination of the tooth germ or the elaboration of the buccal cingulum. The cranium of the examined individual showed some mongoloid morphologic features, too. Our presumption about the formation of the supernumerary tooth may have contributed to the theories of the occurrence of supernumeraries. The sporadic occurrence of this anomaly was reported in recent and archaeological skeletal collections. This study showed that multiple permanent dental formation was present in past Hungarian populations, representing a contribution to the history of dental anomalies. *Dental Anthropology* 2009;22(1):19-22.

Supernumerary teeth are those that are additional to the normal complement (Schulze, 1987). They may occur in any region of the dental arch with a particular predilection for the premaxilla (Primosch, 1981; Nasif *et al*., 1983). This location is followed in decreasing order of frequency by fourth molars or upper distal molars, maxillary paramolars and by lower premolars, upper lateral incisors, lower fourth molars, and lower central incisors. Upper premolars are exceptional, as are upper and lower canines and lower lateral incisors (Gay *et al*., 1999). Supernumerary teeth have been reported in both the primary and the permanent dentitions. Cases involving one or two supernumerary teeth most commonly involve the anterior maxilla (Stafne, 1932), followed by the mandibular premolar region (Nasif *et al*., 1983; Stafne, 1932).

The etiology of supernumerary teeth is still not clearly understood, but several theories have been suggested for their occurrence (Rajab and Hamdan, 2002). For developmental biologists, the phenomenon of supernumerary teeth raises interesting questions about the development and fate of the dental lamina. Also, the supernumerary teeth inspire questions about the actions and interactions of transcription factors and growth factors that coordinate morphogenesis, cell survival and programmed cell death. For clinicians faced with treating the dental complications that arise from the presence of supernumerary teeth, knowledge about the basic mechanisms involved is essential.

Heredity may be a relevant etiological factor in the occurrence of supernumerary teeth (Rajab and Hamdan, 2002). Supernumeraries are more common in the relatives of affected children than in the general population (Garvey *et al*., 1999). The reported prevalence of supernumeraries in the general Caucasian population for the permanent dentition ranges from 0.1 to 3.8% (Rajab and Hamdan, 2002). Supernumerary teeth seem to be more common in Asian populations, with a frequency higher than 3% being reported (Davis, 1987). Sexual dimorphism has been reported by most authors (Hurlen and Humerfelt, 1985; Mitchell, 1989) with males being affected more commonly.

The occurrence of this anomaly is also reported in archeological skeletal collections. Hillebrand (1908) found 14 supernumerary teeth during the paleostomatological investigation of 4,100 skulls. Schwerz (1916) described this anomaly in two out of 510 cases. The sporadic occurrence of supernumeraries in past populations was reported in several other studies

Correspondence to: Gyöngyi Szabó, H-6701 Szeged, P.O. Box 660, Hungary
E-mail: szabo.gyongi@hotmail.com

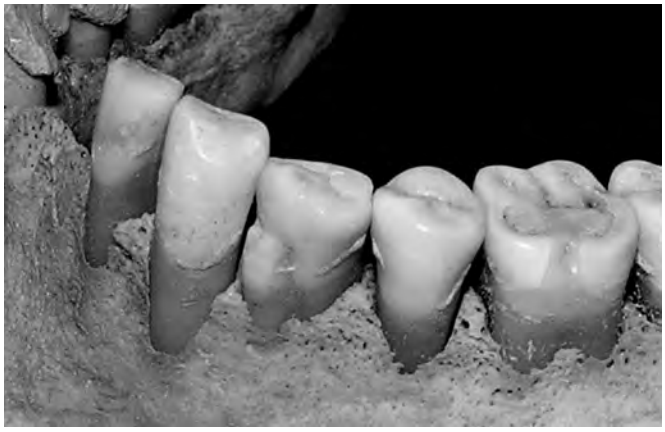

Fig. 1. Joined supernumerary tooth in the left premolar region of mandible.

collected by Kocsis (1993).

This report describes a rare developmental anomaly of a mandibular tooth of a young adult (25-30 yrs) female.

MATERIALS AND METHODS

The material for this report was the skeletal population of Bácsalmás-Óalmás burial site found in a sand pit, where 472 skeletons were excavated from 1993 to 2003. On the basis of the archeological and historical data, this group immigrated from the Balkan Peninsula to the southern part of Hungary in the sixteenth century. For the purpose of this study, the dentitions of 164 well-preserved adult individuals (76 males, 75 females, 13 indeterminate) were examined. Altogether 2,693 teeth (with the exception of the third molars) were used for the investigation. The examination was carried out using macromorphological methods and radiographic analysis. A dial caliper was used for the metric analysis.

RESULTS

During the paleostomatological investigation, altered number of teeth was one of the examined anomalies. The present report is a case of hyperdontia. The lower left first premolar of the young adult female revealed double tooth formation. Only this one case of hyperdontia was found from among the 164 skulls in the skeletal series of Bácsalmás-Óalmás. Due to postmortem loss, the young adult female had no upper left incisors and the upper right central incisor was missing. Pitted hypoplasia on the incisors was seen. Mild periodontal atrophy was

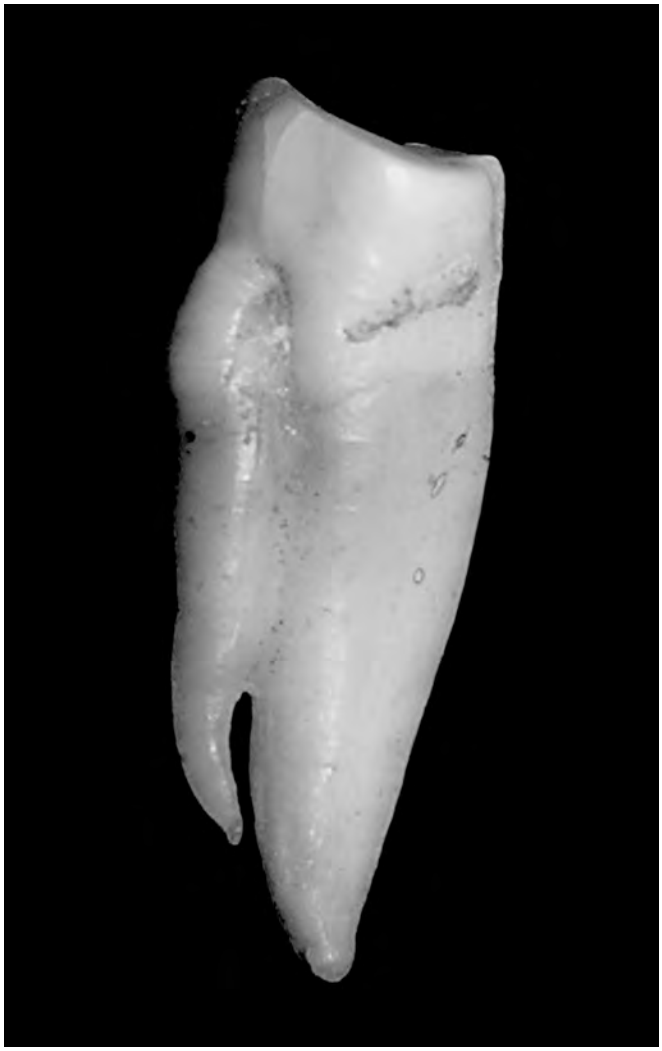

Fig. 2. Distal view of the double tooth formation. Lingual is to the right.

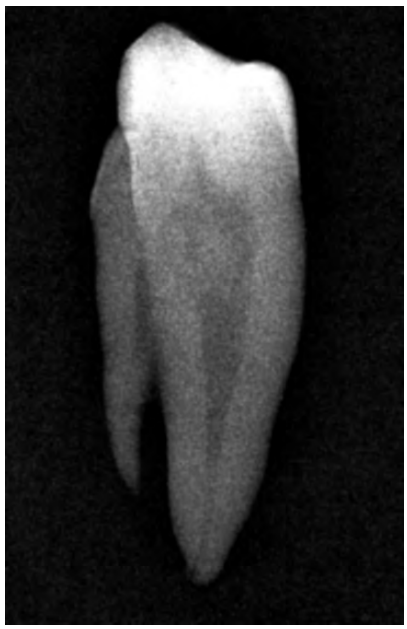

Fig. 3. Mesiodistal radiographic image of the double tooth formation. Lingual is to the right.

evident on the whole dental arch.

On the labial surface of the mandibular first premolar, there is a supernumerary tooth, where the size was definitely smaller than the premolar (Fig. 1, 2). The double tooth displays a bifid crown with a well-defined groove that extends to the distal third of the root. The crown height was 3.64 mm, while that of the premolar-proper was 8.14 mm. The greatest mesiodistal dimension of the accessory crown was 3.22 mm and 7.28 mm for the first premolar. Root length was 10.62 mm and 14.32 mm for the premolar. No anomaly was observed in the right mandibular quadrant, so this represents a unilateral event.

The cranium showed some Mongoloid morphologic features, such as shallow canine fossa and shovel shaped upper incisors. The skeletal remains were well preserved. All of the teeth were found with the exception for the upper left canine, the upper left third molar and the upper right third molar. The status of their alveoli indicates postmortem loss. Different stages of dental caries occurred on the occlusal and mesial surfaces of molars. Caries superficialis were the most common, but a single case of caries penetrans was also observed, on the upper right first molar.

DISCUSSION

Supernumerary teeth may occur singly or in multiples in any region of the jaws in the same person. This study describes a unilateral supernumerary mandibular tooth of an adult female skeleton. Radiographic examination of the fused teeth indicated that the crown of the normal premolar had fused incompletely with the crown of the extra tooth. The fused teeth have two root canals and two partly separate roots. Communication between the pulp chambers of the teeth could be detected radiographically. The position of the extra tooth can be the result of gemination of the first premolar, which means that two morphological units were created by division of the tooth germ. The result is the incomplete formation of two teeth. According to Pindborg (1970), a true concretion develops during the formation of teeth and it is caused by the lack of space. But from another perspective the extra tooth can be the elaboration of the buccal cingulum of the premolar. In support of this concept, the crown is not fused completely and the roots are separated.

Regarding the etiology of this dental anomaly, Rajab and Hamdan (2002) considered heredity as an important etiological factor in the occurrence of supernumerary teeth. Heredity is not conclusive as no other supernumerary was found in this skeletal collection (164 skulls).

The fact that supernumerary teeth are more common in Mongoloid racial groups seems to be conclusive in this case because the investigated skull also shows Mongoloid characteristics.

Clinical complications related to double teeth include caries along the grooves dividing each other and periodontal atrophy, esthetics, and malocclusion (Silva and Silva, 2007). In extant groups, the majority of such teeth are asymptomatic, so endodontic treatment is unnecessary in most cases (Cetinbas *et al*., 2007).

The sporadic occurrence of supernumerary teeth is reported in recent (Hassan *et al*., 2006) and archeological (Sutton, 1985; Smith, 2004) skeletal collections. Kocsis (1993) investigated the permanent frontal teeth of 1,997 individuals originating from different archeological periods of Hungary. He found 23 supernumeraries with a highest frequency in the 10th century AD.

This case report shows that permanent dental formations in the premolar region were also present in the past populations of Hungary, representing a contribution to the history of dental anomalies.

LITERATURE CITED

Cetinbas T, Halil S, Akcam MO, Sari S, Cetiner S. 2007. Hemisection of a fused tooth. Oral Surg Oral Med Oral Path Oral Radiol Endod 104:120-124

Davis PJ. 1987. Hypodontia and hyperdontia of permanent teeth in Hong Kong school children. Community Dent Oral Epidemiol 15:218-220.

D'Souza RN, Klein OD. 2007. Unraveling the molecular mechanisms that lead to supernumerary teeth in mice and men: current concepts and novel approaches. Cells Tissues Organs 186:60-69.

Garvey MT, Berry HJ, Blake M. 1999. Supernumerary teeth—an overview of classification, diagnosis and management. J Can Dent Assoc 61:612-616

Gay C, Mateos M, España A, Gargallo J. 1999. Otras inclusiones dentarias: Mesiodens y otros dientes supernumerarios. Dientes temporales incluidos. In: Gay C, Berini L, editors. Cirugía Bucal. Madrid: Editorial Ergon, Madrid. p 511-550.

Hillebrand J. 1908. Újabb adatok az ember fogainak alaktanához. Budapest: Stephaneum.

Hurlen B, Humerfelt D. 1985. Characteristics of premaxillary hyperodontia: a radiographic study. Acta Odontol Scand 43:75-81.

Kocsis SG. 1993. Investigation of macromorphological developmental anomalies of permanent front teeth from different archaeological periods of Hungary. Thesis, JATE, Department of Anthropology, Szeged [in Hungarian].

Mitchell L. 1989. Supernumerary teeth. Dent Update 16:65-69.

Nasif MM, Ruffalo RC, Zullo T. 1983. Impacted supernumerary teeth: a survey of 50 cases. J Amer Dent Assoc 106:201-204.

Pindborg JJ. 1970. Pathology of the dental hard tissues. San Francisco: WB Saunders Company.

Primosch R. 1981 Anterior supernumerary teeth-assessment and surgical intervention in children. Pediatr

Dent 3:204-215.
Rajab LD, Hamdan MAM. 2002. Supernumerary teeth: review of the literature and survey of 152 cases. Int Peadiatr Dent 12:244-254.
Schulze Ch. 1987. Anomalien und Mißbildungen der menschlichen Zähne. Quintessenz VOL 94-101.
Schwerz F. 1916. Morphologische Untersuchungen an Zähnen von Alamannen aus dem V. bis X. Jahrhundert. Arch Anthropol 15:1-43.
Silva AM, Silva AL. 2007. Unilateral fusion of two primary mandibular teeth: report of a Portuguese archeological case. Dental Anthropology 20:16-18.
Smith P. 2004. Middle bronze age II burials at Sasa, Upper Galilee (Tomb 1 and graves 37, 39). 'Atiqut 46:35-43.
Stafne EC. 1932. Supernumerary teeth. Dental Cosmos 74:653-659.
Sutton PR. 1985. Tooth eruption and migration theories: can they account for the presence of a 13,000-year-old mesiodens in the vault of the palate? Oral Surg Oral Med Oral Path Oral Radiol Endod 59:252-255.

Commentary: Supernumerary teeth

Edward F. Harris

Department of Orthodontics and Department of Pediatric Dentistry, University of Tennessee, Memphis

The case report by Gyongyi Szabó and colleagues (*Dental Anthropology* 2009;22(1):18-21) raises several interesting issues. A challenging aspect of examining teeth—which are the end-products of foregone cascades of developmental events—is that interpretations of the formative processes that produced the final form are conjectural, and there is no way to test assumptions. Experience and encountering repeated occurrences of a dental condition are helpful, but they are hardly infallible.

Terminology

A fundamental consideration raised by this case report is terminology. Specifically, what constitutes a supernumerary tooth? Or, for that matter, what is a tooth? I looked through a number of recent papers on hypo- and hyperdontia, and there is a striking absence of an operational definition of what a "tooth" is. Recognition of a tooth evidently is considered so obvious (or so difficult) that it doesn't warrant a definition. It seems that mineralized tissues (dentin, enamel) are an important criterion, but this is simply because most studies nowadays are radiographic surveys, so premineralized tissues are undetectable. However, dental histologists are quite comfortable that the premineralized structures seen in the bud, cap, and bell stages constitute a "tooth," so mineralization cannot be an essential feature.

Popular textbooks on dental anatomy (*e.g.*, Zeisz and Nuckolls, 1949; Kraus *et al*., 1969; Ash, 1993) launch right into descriptions of the morphology of each tooth type, apparently supposing that a definition would be superfluous. The normally-occurring teeth (20 primary, 32 permanent) are all characterized by a crown (enamel, dentin, pulp) and one or more roots (cementum, dentin, pulp), but it is not clear whether a dental element must have all of these features to achieve "toothness." Also, sizes of the crown and root do not seem to be important criteria. One might claim that teeth obviously are found in the two dental arches, but locality is not definitive given the extraordinary

Fig. 4. A supernumerary tooth in the enlarged incisive foramen of a prehistoric American Indian. Ectopic teeth tend to be in the vicinity of the dental arches, but they may form or migrate elsewhere.

*Correspondence to: Edward F. Harris, Department of Orthodontics, University of Tennessee, Memphis, TN 38163.
E-mail: eharris@utmem.edu

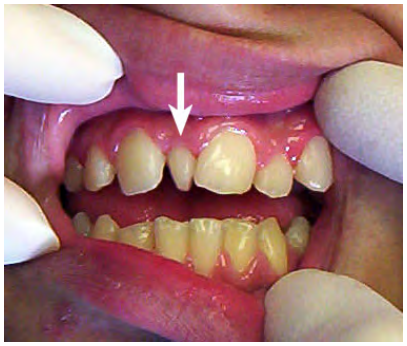

Fig. 5. A mesiodens—a supernumerary tooth located between the maxillary central incisors—is common. Note how this erupted mesiodens displaces the incisors. There is chipping of the occlusal border of the mandibular right central incisor because of the edge-to-edge malocclusion. Supernumerary incisors typically are single-cusped and conical with a single root.

places a "tooth" can occur. Fig. 4‡ is an example where a supernumerary incisor (probably a mesiodens) is hidden in the subject's incisive foramen. The literature describes ectopic teeth located in various midface regions, such as the nasolacrimal duct (Alexandrakis *et al*., 2000), the bony orbit (Savundranayagam, 1972), and the eyelid (Subramaniam *et al*., 1966). Many of us were taught in an embryology class or elsewhere about dermoid cysts (*e.g*., Shafer *et al*., 1983), which contain well-differentiated skin and other identifiable tissues (*e.g*., hair, sweat glands, bone, cartilage, *etc*.), including teeth. These "teeth" commonly are of identifiable types, often incisors and premolars, which shows that the same complex of biochemical signals that produce a tooth in a dental arcade can perform just as well elsewhere in the body (*e.g*., Jernvall and Thesleff, 2000). This is not surprising given the landmark embryological studies

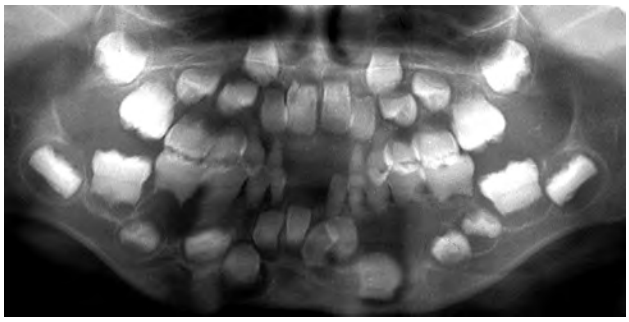

Fig. 6. A cropped view of a panoramic radiograph of a subject with dentin dysplasia I, where root formation is severely restricted, so several of the teeth appear to be 'root-less' though they generally erupt normally. Note the apical radiolucencies around several of the teeth, which is characteristic of this condition. Also, the pulp chambers are obliterated and filled with dysplastic dentin.

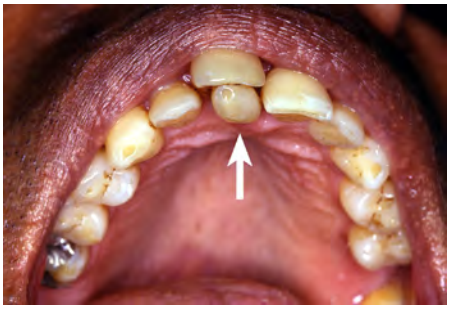

Fig. 7. An exceptionally large tuberculum dentale is located on the subject's right maxillary central incisor (arrow). Large examples such as this with a free cusp often are labeled *talon cusps* because the appearance of an incisor with a labial and lingual cusp is reminiscent of a raptor's claw (*e.g*., Harris and Owsley, 1991). Based on size, this tubercle (with a free apex, a pulp horn, and an independent root) would qualify as a "tooth," but it is not counted as such because (A) it developed from the cingulum of the parent tooth and (B) it is a fused feature of the incisor, sharing dentin and pulp.

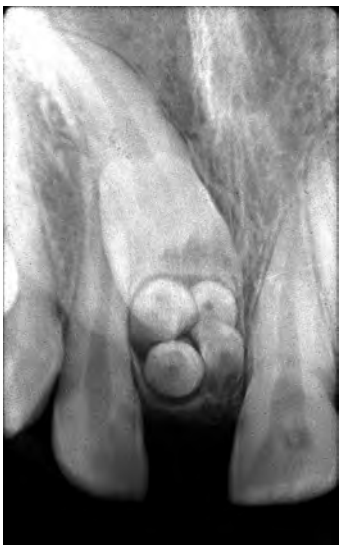

Fig 8. Radiograph of a compound odontoma in the maxillary midline. There are four 'toothlets' visible here, but it is unclear whether they should be labeled as four supernumerary teeth because of their petite size and absence of any crown-root morphology. Even on X-ray, it is evident that these dental elements consist of enamel, dentine, and a pulp chamber. Note how this tumor is preventing the subject's right maxillary central incisor from erupting and how it maintains a several-millimeter gap between the left central and right lateral incisor. Radiograph courtesy of James E. Turner.

‡Figures 1-3 are those in published in the prior article by Szabó *et al*. (2009).

of growing implanted tooth buds in the globes of eyes of laboratory animals (*e.g.*, Yoshikawa and Kollar, 1981). Dermoid cysts occasionally occur in ovaries (*e.g.*, McGinnis and Parham, 1978; Dick and Honoré, 1985; Liberis *et al*. 2008), which means they should be recoverable archeologically, though I'm unaware of any reference to them.

A tooth does not have to be normal size or shape to be counted. Diminutive elements, such as pegged and microdont teeth, are routinely counted. Many authors include mineralized elements of any morphology, including "dental masses" of amorphic mineralized objects as found in odontogenic tumors, notably compound odontomas (*e.g.*, Shafer *et al*., 1983; Owens *et al*., 1997). A supernumerary tooth in the maxillary incisor region is probably the most common sort of supernumerary tooth, and these are characteristically petite single-cusped, often conical teeth with a single root (Fig. 5).

Once mineralized, a "tooth" normally has a crown and root, but there are exceptions: A primary tooth in which the root has been completely lysed as part of the exfoliation process is still considered a tooth. So-called root-less teeth (as in dentin dysplasia I; OMIM #125400) also are considered teeth, though roots can be quite abbreviated if present (Fig. 6). Size alone does not define a tooth. The lingual tubercle (talon cusp) in Figure 7 is virtually as large as the incisor crown proper, but it would not be counted as a tooth because (1) it is developmentally a component of that incisor and (2) it has always been united with the incisor. At the other extreme, Figure 8 shows a compound odontoma (de Oliveira *et al*., 2001), where four distinct tooth-like 'denticles' are evident (with the normal but impacted central incisor apical to them). Do these 'toothlets' qualify as teeth? They have fully-differentiated enamel and dentin, but no crown-and-root morphology.

Does a "tooth" need to be physically separate from others to be counted? This seems to be an important distinction implied in most studies (Patterson, 1956; Hershkovitz, 1967). For example, cusp-like cingular elements are not counted as teeth. Tubercles, accessory cusps, and styles are considered parts of the main tooth. Cingular elements can be fairly large, but they are almost invariably coalesced with the permanent tooth so there should be no misidentification. These include talon cusps on the incisors, tuberculum dentale on canines, Carabelli's cusps on the lingual of upper molars, and paramolar tubercles on the buccal aspect of upper and lower molars (Scott and Turner, 1997). All of these cingular elements normally are single-cusped, and they all have at most a single root (*e.g.*, Bolk, 1916). Ambiguity arises when, apparently in rare instances, a dental feature becomes physically separated from the main tooth (Dubuk *et al*., 1996). Paramolar tubercles do occasionally achieve physical independence when large, and these meet criteria for a "tooth," namely possession a crown (enamel), root (dentin), and a tooth-like morphology (though simplified).

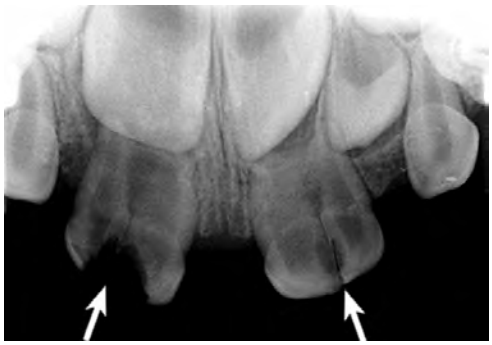

Fig. 9. A rare instance of bilateral fusion of the primary maxillary incisors (arrows). (Most cases are unilateral.) Fusion is confirmed by (A) the appearance of confluent tooth forms in each quadrant and (B) the 'absence' of independent lateral incisor teeth. Both compound teeth are carious, but their shared enamel, pulp chambers, and root dentin are evident. Radiograph courtesy of Ann S. Smith.

Overlooking the details of what constitutes a tooth, there are countless anthropological and clinical dental studies of abnormal tooth numbers—either the congenital absence of one or more teeth (hypodontia) or hyperdontia, an excess number of teeth (Table 1). Studies rarely press the definition of a tooth too closely; instead, wording is used such as: hypodontia is a deficit in the normal dental formula or hyperdontia is teeth in excess of the normal dental complement.

TABLE 1. Operational definitions[1]

Condition	Definition
Hypodontia	Congenital absence of one to five permanent teeth, generally excluding third molars.
Oligodontia	Absence of more than five teeth. The study may or may not exclude third molars.
Anodontia	The complete absence of all primary and/or permanent teeth. The phrase "partial anodontia" (actually denoting hypodontia or oligodontia) is an oxymoron.
Hyperdontia	Presence of one or more teeth in excess of the species' normal dental formula.

[1]Partly from Schalk van der Weide (1992), reproduced in Koch and Thesleff (2001, p 261).

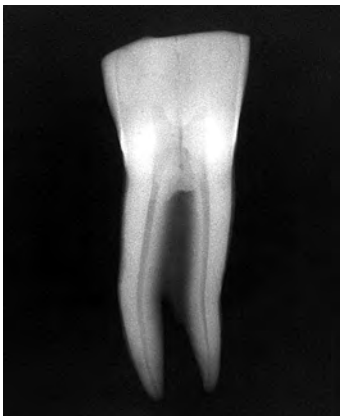

Fig. 10. Radiograph showing fusion between a lower right central and lateral incisor (labial view). The lateral incisor is to the left of the figure. Note the confluence of enamel and dentin between the crowns, though the pulp chambers and roots are separate.

Ontogeny

The structure imaged in Szabó's figures clearly emanates from the premolar's buccal cingulum, and it shows developmental features in common with the tooth proper. As Szabó *et al*. point out, there is a common pulp chamber, and the dentin is confluent between the tooth crown proper and the tubercle even though the tubercle has a well-developed root and pulp chamber (Ohishi *et al*., 1999). It is most probable that this cingular feature was initiated by an enamel knot that, in the presumptive tooth, was located at the cusp apex, which has now (Fig. 2) been abraded or is hidden by subsequent enamel deposition. A primary enamel knot is essential for a tooth's formation, and later-forming secondary knots define each of a tooth's cusps (*e.g*., Jernvall *et al*., 1994; Thesleff and Jernvall, 1997;

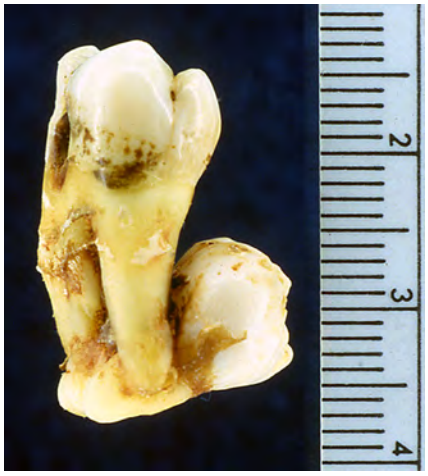

Fig. 11. Example of acquired concrescence between a second and third molar. Roots of the two teeth are only united by cementum; there is no confluence of the underlying dentin.

Fig. 12. A paramolar tubercle on a maxillary left second molar. This tubercle (arrow) clearly is associated with the metacone rather than the molar's paracone. Bolk (1916) was very keen that paramolar tubercles were only derived from the paracone, though Kustaloglu (1962) showed that this is untrue.

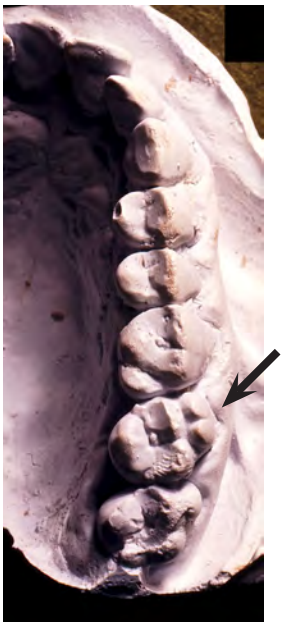

Fig. 13. A rare instance of two paramolar tubercles on a maxillary left second molar (arrow). (No cingular feature could be seen on the contralateral molar.) It appears that both tubercles are attached to the paracone (mesiobuccal cusp), though part of the distal tubercle crosses onto the metacone. Note too a large, single paramolar tubercle on the paracone of the third molar. (Paramolar tubercles rarely occur on permanent first molars.)

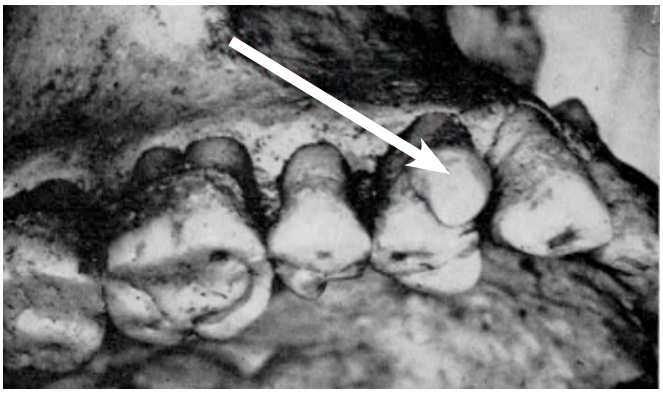

Fig. 14. A large parastyle on the maxillary right first premolar (line). A parastyle is a tubercle derived from the buccal cingulum of, in this case, the premolar's paracone. (From Kustaloglu, 1962.)

Thesleff *et al*., 2001; Obara and Lesot 2007). I think it is notable that this cingular feature has a free apex that is occlusal to the developmental groove that distinguishes this tubercle from the tooth proper; this shows that the tubercle was developed as part of the differentiating morphology of the inner enamel epithelium because mineralization of dentin and enamel only proceeds in the occlusal-to-apical direction.

These morphological components that are developmental parts of a tooth are not considered as separate teeth in tooth counts. Ambiguous cases occur when a feature that is supposed to arise from an adjacent tooth's cingulum is a physically separate dental element. Bolk (1916) describes such cases in his classic paper on paramolar tubercles. Either of two events may cause this, though the end products seem identical. One, the secondary enamel knot may have formed far enough away from the rest of the crown that the tubercle fissions off from the main tooth. This process of gemination (the word is derived from Gemini, the star constellation of twins in Greek mythology) is commonly described in dental texts on dental anomalies (*e.g*., Pindborg, 1970; Shafer *et al*., 1983), though actual examples of twinning are rare (*e.g*., Gündüz and Açikgõz, 2006; Sivolella *et al*., 2008). Twinning needs to occur during the cap or bell stage prior to crown mineralization, but the actual process is not understood. A critical feature defining geminated teeth is the presence of all of the other teeth in the morphogenetic field, so the twinned teeth clearly are not fused teeth (Fig. 9). Twinning requires duplication of the biochemical signals for tooth development within the dental sac. How this occurs seems to be a complete mystery at present. A traditional view is that two tooth-forming sites are stimulated to form close together in the dental lamina, which develops well before differentiation of the dental sac. It is supposed (Pispa and Thesleff, 2003) that, in normal dental development, a reaction-diffusion gradient develops around a formative teeth, where activators induce placode formation while negative regulators are intensified in interplacodal regions, which inhibit tooth formation and, thus, account for the orderly spacing of teeth. Gemination might, then, be viewed as an exception where two sets of signals are preserved (or initiated) within the same dental sac that, then, gives rise to 'twinned' but fused teeth. Geminated teeth (more common in the primary dentition) usually have a shared root and shared pulp cavity.

The second process involves fusion, where two tooth buds begin to form independently, but, again, for reasons unknown, the formative teeth grow together. Fusion typically starts at the cap or bell stage, so that the united teeth are combined along the lengths of their crowns and roots (Fig. 10). Fusion must involve the dentin, so the twinning is initiated during formation of the outer enamel epithelium (Avery, 1994). The key feature for identification is that, counting the fused pair of elements as one, there needs to be a 'missing' tooth elsewhere in that morphogenetic field. This method of defining fusion is not thorough-going, because it supposes that development was disruptive enough to meld two tooth buds, but the same disruption did not cause agenesis of the "missing" tooth. Reliance on the fused tooth morphology can be a help here, but convincing discrimination between fission and fusion may be impossible from inspection of the end product alone.

A rare but classic case of tooth fusion is in people (and laboratory animals) with developmental midline problems, notably holoprosencephaly (HPE). HPE is the embryological failure of divisions of the head to form along the left-right, transverse, and/or craniocaudal axes (Cohen, 2001). A remarkable dental consequence of this heterogenous group of anomalies can be a solitary median maxillary central incisor (SMMCI). Nanni *et al*. (2001) provide a current review of this condition. Experimental work shows that sonic hedgehog (shh), a signaling protein, is critical for the initiation of a tooth germ, probably by directing epithelial cell proliferation. In mice, the absence of shh can either prevent maxillary incisor formation (congenital absence) or cause these incisors to fuse. The maxillary central incisors begin formation close together and these tooth germs coalesce into a single symmetric central incisor (Hardcastle *et a*l., 1998). Of note, the molar teeth are unaffected. Alterations in the structure-function of shh provide the common etiology between the head (central nervous system) and tooth anomalies (Cohen, 2004).

Aside from fusion and fission (gemination), yet a third situation occasionally occurs, namely concresence. Pindborg (1970) valuably distinguishes between true concrescence and acquired concrescence. Acquired concrescence occurs when two fully formed teeth are only united by the fluorescence of cementum (Fig. 11). Colby *et al*. (1961:42) note that two factors are required here, (1) the teeth, specifically the roots, of adjacent teeth

need to be in close proximity and (2) hypercementosis—excessive cementum deposition—unites the proximate roots. Acquired concrescence is only distantly related to the fission and fusion of teeth because it occurs after tooth formation in contrast to being the consequence of some developmental aberration. In contrast, true concrescence involves confluence of the roots (dentin) of adjacent teeth, so it is a sort of fusion.

Paramolar tubercles

Numerous researchers have described "paramolar tubercles," a term coined by Bolk (1916:110). Bolk surveyed some 30,000 skulls, so he is still a contender for the record number of identified tubercles. Bolk argued that these tubercles on maxillary molars always develop from the mesial cusp. In fact, they can arise from the cingulum of either buccal cusp, and Kustaloglu (1962) notes that they therefore should be labeled parastyles (mesiobuccal) or metastyles (distobuccal) depending on the cusp of origin. Figure 12 shows a characteristic expression, where the tubercle developed buccal to the metacone, well distal of the lingual developmental groove that demarcates the union of the paracone and metacone. Figure 13 shows a second molar with two equal-size paramolar tubercles, and it appears that both developed from the tooth's paracone.

Such buccal tubercles are less common in the mandible, where, occasionally, they develop from the mesiobuccal cusp, thus making them protostylids (*e.g.*, Dahlberg, 1950). Protostylids occur frequently enough that there is an ASU dental plaque to score their size (Turner *et al.*, 1991; also see Hlusko, 2007; Skinner *et al.*, 2008). Paramolar features also can occur on the premolars. Figure 14 is reproduced from Kustaloglu's article, showing a large tubercle on the facial aspect of the paracone (buccal cusp) of a maxillary premolar; this example is not dissimilar from the example described by Szabó and coworkers (Fig. 1).

Hyperdontia

Various ideas have been put forth over the years to explain why a supernumerary tooth might occur. Some of these are noted in the reviews by Rajab and Hamdan (2002), Botra *et al.* (2005), and elsewhere. These conjectures are of historical interest, but they comport poorly with current knowledge of the molecular control of tooth formation (*e.g.*, Mitsiadis and Smith, 2006). A popular idea was atavisim, which is the idea that some phylogenetic ancestral condition (where more teeth were the norm) is being re-expressed. Recall, for instance, that the baseline mammalian condition was at least 44 teeth (Gregory, 1922; Ji *et al.*, 2002), and the human dental formula involves reductions of all tooth types except the canines (see review by Peterkova *et al.*, 2006). Another conjecture was that one or more of the normally-occurring teeth splits (the dichotomy theory) to produce additional teeth (Foley and Del Rió, 1970; Taylor, 1972). Another idea with some persistent credibility involves an extension of dental lamina at the end of the tooth row that is induced to form an additional tooth (Saarenmaa, 1951), but this idea must include the reciprocal epithelial-mesenchymal inductions that promote tooth formation, "extra" dental lamina in itself does not cause teeth to form. Such historical conjectures suppose that extra teeth are due to additional developmental activity, with the term "hyperactivity" often used in some vague sense to explain the over-production of teeth.

Recent evidence suggests that the opposite is true—that biochemical signaling is responsible for *stopping* the enumeration of teeth and is necessary for holding a species' dental formula in check. A prime example is now known in some detail for humans: Runx2 is a transcription factor that is key for osteogenic cell differentiation (Ziros *et al.*, 2008). Mutations of Runx2, which also is known as Cbfa1, can cause cleidocranial dysostosis (CCD; OMIM #119600), the condition that is, perhaps, archetypical of hyperdontia in man (Jensen and Kreiborg, 1990; Whittington and Durward, 1996). People with CCD are likely to exhibit hyperdontia, especially in the premolar region (along with systemic problems of non-eruption due to a failure of bone resorption ahead of the erupting tooth). CCD shows the important role that Runx2 normally plays in *preventing* excess budding of the dental lamina. However, hyperdontia in people with this autosomal dominant allele show variable expressivity, ranging from no extra teeth to cases with numerous extra teeth. The percentage of cases of CCD with hyperondia is around 1/5, showing that even in this archetypical condition, the formation of extra teeth is uncertain—presumably due to differences in allelic conditions and differences in genetic backgrounds.

Comparably, Kantaputra and coworkers (2008) describe a single subject with unerupted teeth in the premolar-molar region evidently due to an inherited defect in Trps1 causing gain of function. These authors suggest that this mutation mimics the dental phenotype of persons with Runx2.

Murashima-Suginami *et al.* (2007, 2008) show that up-regulated bone morphogenetic protein (BMP) signaling causes supernumerary tooth formation in mice, notably in the incisor region (also see Kassai *et al.* 2005). They interpret their experimental results as showing that odontogenic mesenchymal cells normally are killed off at the end of tooth rows because antagonists to BMP play a crucial role in controlling the enumeration of tooth buds. When an antagonist (termed ectodin or, synonymously, "uterine sensitization associated gene-1" or USAG-1) is absent, BMP function is left uncontrolled, and the result is supernumerary tooth formation. That is, ectodin normally binds to BMP

and inhibits its function; without inhibition, BMP can promote additional tooth sites.

These studies show that extra teeth result from inadequate suppression of tooth-forming capacity, not the over-activity of tooth-promoting events.

At this point in our understanding of tooth-promoting conditions, it is unknown (A) how many genes (alleles, proteins) are responsible along the involved pathway of tooth development either to form an extra tooth or curtail formation of a normal tooth, (B) whether extra teeth at the end of the dental lamina (*e.g.*, mesiodens, fourth molars) are due to the same causes as those within the tooth rows (such as the common extra premolars). Other issues of interest involve (A) how and why human population differences in hypo- and hyperdontia have developed, (B) what causes the persistent sex differences (hypodontia is more common in females; hyperdontia is more common in males) seen among humans, and (C) why the locations of missing and extra teeth differ among human groups. It also is effectively unknown how the environment affects any or all of these differences. It seems unlikely that there are simple or single, all-inclusive reasons for any of these issues. It is noteworthy that most supernumerary teeth are few in number within and among subjects, undersize and morphologically simplified. Overall, it seems to be a major genotypic effort to increase tooth number, perhaps because of the large number of necessary steps needed to form a tooth.

Studies of supernumerary teeth in laboratory animals have certainly been informative (D'Souza and Klein, 2007). Several studies show that perturbations of signalling molecules—either genetic knockouts or the overproduction of certain molecules—can cause the formation of extra teeth. For example, mice that over-express ectodysplasin (Pispa *et al.*, 2004) or under-express antagonists to FGF (fibroblast growth factor; Klein *et al.*, 2006) can produce supernumerary teeth. But, it is important to question the relevance of these findings to humans. Mice—the favored animal for studying tooth development—have a diastema in each quadrant where formation of lateral incisors, canines, and premolars is suppressed. However, several of these teeth initiate formation but are arrested and resorbed in the bud stage (Peterkova *et al.* 2002, 2006) so the "rescue" of these tooth buds to permit them to develop into "supernumerary diastema teeth" is of considerable interest, but it is fundamentally different from the human condition where no primordia normally form.

Laterality

Another question raised by Szabó's case report is why their tubercle occurs unilaterally. Conventional wisdom is that the genotypic information is the same in the left and right hemispheres of the body (Polak 2003), so disparate phenotypes between quadrants are supposed to be the exception rather than the rule. Researchers familiar with dental morphology recognize that, while left-right symmetry may be the norm, even striking exceptions are not hard to find. Alvesalo and coworkers (1975) suggested that, for Carabelli's trait, expression on one tooth is always associated with some expression on the contralateral tooth, but this has not been my own experience. Kustaloglu (1962) examined the osteological collections at the Chicago National History Museum (roughly 500 individuals) and found that paramolar tubercles tend to occur unilaterally more often than bilaterally, with a ratio of 18:4 among the permanent molars, though bilateral occurrences predominated in the primary dentition.

Dental anthropologists have embraced the idea that morphologic dental traits have a quasicontinuous mode of inheritance. Supporting evidence stems primarily from animal studies (*e.g.*, Grüneberg, 1950, 1952) because few anthropological studies have subjects of known biological relationship (*cf.* Saunders and Mayhall, 1982; Sjøvold, 1996). The quasicontinuous (QC) model of inheritance suggests that morphological dental traits are under polygenic control, but with a threshold below which the feature is not expressed (Wright, 1934a,b; Falconer, 1965). The question arises whether unilateral expression (Fig. 1) is indicative of the subject's genotype being close to the threshold. That is, subjects with a genotype for trait expression might be prone to expressing the trait unilaterally due to local environmental vagaries between the jaw's quadrants. Supposition is that genotypes farther above the threshold would be more likely to exhibit bilateral symmetry. This aspect of a QC model does not seem to have been tested for dental traits.

OVERVIEW

In sum, my contention is that the case described by Szabó and coworkers is a paramolar tubercle on the lower left first premolar, and, thus, should be labeled a protostylid. It is possible that this cingular feature developed from local trauma or infection, which would account for its unilateral expression, though that is sheer speculation. This tubercle is unquestionably a developmental feature of the premolar itself, as its union (shared enamel, dentin, and pulp cavity) precludes it being a supernumerary tooth.

These comments are set forth in hopes of stimulating discussion among readers regarding this interesting case.

LITERATURE CITED

Alexandrakis G, Hubbell RN, Aitken PA. 2000. Naso-lacrimal duct obstruction secondary to ectopic teeth. Ophthalmology 107:189-192.

Alvesalo L, Nuutila M, Portin P. 1975. The cusp of Carabelli: occurrence in first upper molars and evaluation

of its heritability. Acta Odontol Scand 33:191-197.
Ash MM Jr. Wheeler's dental anatomy, physiology and occlusion, 7th ed. Philadelphia: WB Saunders, 1993.
Avery JK. 1994. Oral development and histology, 2nd ed. New York: Thieme Medical Publishers, Inc.
Bolk L. 1916. Problems of human dentition. Am J Anat 19:91-148.
Cohen MM Jr. 2001. On the definition of holoprosencephaly. Am J Med Genet 103:183–187.
Cohen MM Jr. 2004. SHH and holoprosencephaly. In: Epstein CJ, Erickson RP, Wynshaw-Boris A, editors. In: Inborn errors of development. New York: Oxford University Press. p 240–248.
Colby Ra, Kerr DA, Robinson HBG. 1961. Color atlas of oral pathology, 3rd ed. Philadelphia: JB Lippincott Company.
Dahlberg AA. 1950. The evolutionary significance of the protostylid. Am J Phys Anthropol 8:15-25.
Dick HM, Honoré LH. 1985. Dental structures in benign ovarian cystic teratomas (dermoid cysts). A study of ten cases with a review of the literature. Oral Surg Oral Med Oral Pathol 60:299-307.
D'Souza RN, Klein OD. 2007. Unraveling the molecular mechanisms that lead to supernumerary teeth in mice and men: current concepts and novel approaches. Cells Tissues Organs186:60-69.
Dubuk AN, Selvig KA, Tellefsen G, Wikesjö UM. 1996. Atypically located paramolar. Report of a rare case. Eur J Oral Sci 104:138-140.
Falconer DS. 1965. The inheritance of liability to certain diseases, estimated from the incidence among relatives. Ann Hum Genet 29:51-71.
Foley MF, Del Rió CE. 1970. Supernumerary teeth: report of a case. Oral Surg Oral Med Oral Pathol 30:60-63.
Gregory WK. 1922. The origin and evolution of the human dentition. Baltimore: Williams and Wilkins Company.
Grüneberg H. 1950. Genetical studies on the skeleton of the mouse. I. Minor variations of the vertebral column. J Genet 50:112-141.
Grüneberg H. 1952. Genetical studies on the skeleton of the mouse. IV. Quasi-continuous variations. J Genetic 51:95-114.
Gündüz K, Açikgõz A. 2006. An unusual case of talon cusp on a geminated tooth. Braz Dent J 17:343-346.
Hardcastle Z, Mo R, Hui CC, Sharpe PT. 1998. The Shh signalling pathway in tooth development: defects in Gli2 and Gli3 mutants. Development 125:2803-2811.
Harris EF, Owsley DW. 1991. The talon cusp: a review with three cases from native North America. J Tennessee Dent Assoc 71:20-22.
Hershkovitz P. 1967. Dynamics of rodent molar evolution: a study based on new word Cricetinae, family Muridae. J Dent Res 46 (Suppl. 5):829–842.
Hlusko LJ. 2007. 2004. Protostylid variation in Australopithecus. J Hum Evol 46:579-594.
Jensen BL, Kreiborg S. 1990. Development of the dentition in cleidocranial dysplasia. J Oral Pathol Med 19:89-93.
Jernvall J, Kettunen P, Karavanova I, Martin LB, Thesleff I. 1994. Evidence for the role of the enamel knot as a control center in mammalian tooth cusp formation: non-dividing cells express growth stimulating Fgf-4 gene. Int J Dev Biol 38:463-469.
Jernvall J, Thesleff I. 2000. Reiterative signaling and patterning during mammalian tooth morphogenesis. Mech Dev 92:19-29.
Ji Q, Luo ZX, Yuan CX, Wible JR, Zhang JP, Georgi JA.2002. The earliest known eutherian mammal. Nature 416:816-822.
Kantaputra P, Miletich I, Lüdecke HJ, Suzuki EY, Praphanphoj V, Shivdasani R, Wuelling M, Vortkamp A, Napierala D, Sharpe PT. 2008. Tricho-rhino-phalangeal syndrome with supernumerary teeth. J Dent Res 87:1027-1031.
Kassai Y, Munne P, Hotta Y, Penttilä E, Kavanagh K, Ohbayashi N, Takada S, Thesleff I, Jernvall J, Itoh N. 2005. Regulation of mammalian tooth cusp patterning by ectodin. Science 309:2067-2070.
Klein OD, Minowada G, Peterkova R, Kangas A, Yu BD, Lesot H, Peterka M, Jernvall J, Martin GR. 2006. Sprouty genes control tooth number via bidirectional antagonism of epithelial-mesenchymal FGF signaling. Dev Cell 11:181-190.
Koch G, Thesleff I. 2001. Developmental disturbances in number and shape of teeth and their treatment. In: Koch G, Poulsen S, editors. Pediatric dentistry—a clinical approach. Copenhagen: Munksgaard. p 253-271.
Kraus BS, Jordan RE, Abrams L. 1969. Dental anatomy and occlusion: a study of the masticatory system. Baltimore: Williams & Wilkinson.
Kustaloglu OA. 1962. Paramolar structures of the upper dentition. J Dent Res 41:75-83.
Liberis V, Tsikouras P, Sivridis E, Dadidou M, Koutlaki N, Galazios G. 2008. Irregular dental structures in a benign ovarian cystic teratoma (dermoid cyst): case report. Clin Exp Obstet Gynecol 35:151-152.
McGinnis JP Jr, Parham DM. 1978. Mandible-like structure with teeth in an ovarian cystic teratoma. Oral Surg Oral Med Oral Pathol 45:104-106.
Mitsiadis TA, Smith MM. 2006. How do genes make teeth to order through development? J Exp Zoolog B Mol Dev Evol 306:177-182.
Murashima-Suginami A, Takahashi K, Kawabata T, Sakata T, Tsukamoto H, Sugai M, Yanagita M, Shimizu A, Sakurai T, Slavkin HC, Bessho K. 2007. Rudiment incisors survive and erupt as supernumerary teeth as a result of USAG-1 abrogation. Biochem Biophys Res Commun 359:549-555.
Murashima-Suginami A, Takahashi K, Sakata T, Tsukamoto H, Sugai M, Yanagita M, Shimizu A, Sakurai T, Slavkin HC, Bessho K. 2008. Enhanced BMP signaling results in supernumerary tooth formation in USAG-1 deficient mouse. Biochem Biophys Res Commun

369:1012-1016.
Nanni L, Ming JE, Du Y, Hall RK, Aldred M, Bankier A, Muenke M. 2001. SHH mutation is associated with solitary median maxillary central incisor: a study of 13 patients and review of the literature. Am J Med Genet 102:1-10.
Obara N, Lesot H. 2007. Asymmetrical growth, differential cell proliferation, and dynamic cell rearrangement underlie epithelial morphogenesis in mouse molar development. Cell Tissue Res 330:461-473.
Ohishi K, Ohishi M, Takahashi A, Kido J, Uemura S, Nagata T. 1999. Examination of the roots of paramolar tubercles with computed tomography: report of 3 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 88:479-483.
de Oliveira BH, Campos V, Marçal S. 2001. Compound odontoma—diagnosis and treatment: three case reports. Pediatr Dent 23:151-157.
Owens BM, Schuman NJ, Mincer HH, Turner JE, Oliver FM. 1997. Dental odontomas: a retrospective study of 104 cases. J Clin Pediatr Dent 21:261-264.
Patterson B. 1956. Early Cretaceous mammals and the evolution of mammalian molar teeth. Fieldiana: Geol 13:1-105.
Peterkova R, Lesot H, Peterka M. 2006. Phylogenetic memory of developing mammalian dentition. J Exp Zoolog B Mol Dev Evol 306:234-250.
Peterkova R, Peterka M, Viriot L, Lesot H. 2000. Dentition development and budding morphogenesis. J Craniofac Genet Dev Biol 20:158-172.
Peterkova R, Peterka M, Viriot L, Lesot H. 2002. Development of the vestigial tooth primordia as part of mouse odontogenesis. Connect Tissue Res 43:120-128.
Pindborg JJ. 1970. Pathology of the dental hard tissues. San Francisco: WB Saunders Company.
Pispa J, Thesleff I. 2003. Mechanisms of ectodermal organogenesis. Dev Biol 262:195-205.
Pispa J, Mustonen T, Mikkola ML, Kangas AT, Koppinen P, Lukinmaa PL, Jernvall J, Thesleff I. 2004. Tooth patterning and enamel formation can be manipulated by misexpression of TNF receptor Edar. Dev Dyn 231:432-440.
Polak M, ed. 2003. Developmental instability: causes and consequences. Oxford: Oxford University Press.
Rajab LD, Hamdan MAM. 2002. Supernumerary teeth: review of the literature and survey of 152 cases. Int Peadiatr Dent 12:244-254.
Saarenmaa SL. 1951. The origin of supernumerary teeth. Acta Odontol Scand 9:293-303.
Saunders SR, Mayhall JT. 1982. Developmental patterns of human dental morphological traits. Arch Oral Biol 27:45-49.
Savundranayagam A. 1972. A migratory third molar erupting into the lower border of orbit causing blindness in the left eye. Aust Dent J 17:418-420.
Schalk van der Weide Y. 1992. Oligodontia: a clinical, radiographic and genetic evaluation. Ph.D. dissertation, University of Utrecht, The Netherlands.
Scott GR, Turner CG II. 1997. The anthropology of modern human teeth: dental morphology and its variation in recent human populations. Cambridge: Cambridge University Press.
Shafer WG, Hine MK, Levy BM. 1983. A textbook of oral pathology, 4th ed. Philadelphia: WB Saunders.
Sivolella S, Bressan E, Mirabal V, Stellini E, Berengo M. 2008. Extraoral endodontic treatment, odontotomy and intentional replantation of a double maxillary lateral permanent incisor: case report and 6-year follow-up. Int Endod J 41:538-546
Sjøvold T. 1996. Testing assumptions for skeletal studies by means of identified skulls from Hallstatt, Austria. In: Saunders SR, Herring A, editors. Grave reflections: portraying the past through cemetery studies. Toronto: Canadian Scholars' Press Inc, p 241-281.
Skinner MM, Wood BA, Boesch C, Olejniczak AJ, Rosas A, Smith TM, Hublin JJ. 2008. Dental trait expression at the enamel-dentine junction of lower molars in extant and fossil hominoids. J Hum Evol 54:173-186.
Subramaniam KS, Prabhakaran M, Premalatha R. 1966. Ectopic teeth in eyelid. Arch Ophthalmol 75:810-811.
Taylor GS. 1972. Characteristics of supernumerary teeth in the primary and permanent dentition. Dent Pract Dent Rec 22:203-208.
Thesleff I, Jernvall J. 1997. The enamel knot: a putative signaling center regulating tooth development. Cold Spring Harb Symp Quant Biol 62:257-267.
Thesleff I, Keranen S, Jernvall J. 2001. Enamel knots as signaling centers linking tooth morphogenesis and odontoblast differentiation. Adv Dent Res 15:14-18.
Turner II CG, Nichol CR, Scott GR. 1991. Scoring procedures for key morphological traits of the permanent dentition: The Arizona State University Dental Anthropology System. In: Kelley MA, Larsen CS, editors. Advances in dental anthropology. New York: Wiley-Liss Inc. p 13-31.
Whittington BR, Durward CS. 1996. Survey of anomalies in primary teeth and their correlation with the permanent dentition. N Z Dent J 92:4-8.
Wright S. 1934a. An analysis of variability in number of digits in an inbred strain of guinea pigs. Genetics 19:506-536.
Wright S. 1934b. The results of cross between inbred strains of guinea pigs differing in number of digits. Genetics 19:537-551.
Yoshikawa DK, Kollar EJ. 1981. Recombination experiments on the odontogenic roles of mouse dental papilla and dental sac tissues in ocular grafts. Arch Oral Biol 26:303-307.
Zeisz RC, Nuckolls J. 1949. Dental anatomy. St Louis: CV Mosby Company.
Ziros PG, Basdra EK, Papavassiliou AG. 2008. Runx2: of bone and stretch. Int J Biochem Cell Biol 40:1659-63.

Dental Perspectives on Human Evolution: State-of-the-Art Research in Dental Paleoanthropology. 2007. Edited by Shara E. Bailey and Jean-Jacques Hublin. Vertebrate Paleobiology and Paleoanthropology Series. Dordrecht, The Netherlands: Springer (403 pages + index). $129.00, ISBN: 978-1-4020-5844-8

This is the third book in Springer's series on Vertebrate Paleobiology and Paleoanthropology; it consists of the proceedings of the first symposium on Human Evolution held at the Max Planck Institute for Evolutionary Anthropology (Leipzig, Germany). The volume illustrates the diverse and innovative ways that teeth inform our understanding of human evolution. Recent advances in the analysis of dental morphology, microstructure, development, and wear are showcased with respect to how they have increased knowledge of hominin phylogeny, ontogeny, and adaptation to changing dietary environments. An introduction to the volume by Simon Hillson provides a synopsis of key themes and unique perspectives presented in each chapter. The four main sections of the volume begin with an introductory chapter by scholars that have made a significant impact on the field. These introductions provide useful analytical summaries of each contribution and place them in the broader context of research in dental anthropology and paleoanthropology. Some, such as Fred Grine's introduction to Part IV: 'Dentition and Diet', which focuses on dental macro- and micro-wear, is comprehensive, historical, and well referenced - with 135 citations. Others, including Wood's introduction to Part III: 'Dental Development' are brief, yet highlight key features of each chapter in the section. A bit perplexing is Macchiarelli and Bailey's introduction to Part II: 'Dental microstructure and life history', where on several occasions the reader is uncertain which author's observations and opinions are being presented ('in my view', 'I would also like to note', 'in my personal view'). A brief synopsis of each of four section of the volume follows.

Part I: 'Dental evolution and dental morphology', contains seven chapters, and begins with Pilbrow's analysis of occlusal odontometric variation in great ape molar teeth. Results indicate that great ape molar metrics exhibit patterns of inter-species and sub-species taxonomic diversity. Despite small sample sizes, lack of understanding of inter-trait associations, and use of a classification system designed for scoring modern human tooth crown morphology, Bailey and Wood explore the evolutionary divergence of the Homo and Paranthropus lineages using post-canine morphometric variation. They find that increased dental crown complexity in Paranthropus is not a primitive retention and that dental trends said to be characteristic of Homo actually appear relatively late in human evolution. Maxillary molar cusp morphology of South African australopithecines is analyzed by Moggi-Cecchi and Boccone who find similarities (in crown base areas) and significant differences (in relative area of anterior cusps and molar size sequences) between A. africanus and A. robustus. Crown morphology of fossil samples from Gran Dolina (TD-6) and Sima de los Huesos are used by Martinón-Torres and colleagues, to assess phylogenetic issues related to the early colonization of Europe. They conclude that a coordinated assessment using biological and cultural evidence holds promise.

An innovative technique—neural network analysis using Self Organizing Maps—for describing dental morphology is used by Manni and colleagues to evaluate the relationship between archaic and modern Homo sapiens. Though it has some advantages, this new technique may have limitations that preclude its adoption by other investigators. The final two chapters in Part I focus on exciting new, non-destructive advances in imaging dental structures and tissues. Olejniczak and associates discuss methodological aspects of 3D data acquisition by micro-computed tomography of primate molar teeth. Precise and reliable portrayal of the enamel-dentine junction and measures of enamel cap thickness are tightly linked to methodological parameters such as slice thickness and pixel resolution. The advantages of high resolution X-ray computer tomography (HRXCT) for obtaining digital 3D data and volumetric properties of dense tissues, is reviewed by Gantt and colleagues.

Five chapters comprise Part II: 'Dental microstructure and life history.' This section begins with an analysis of dental microstructure, growth and life history of Megaladapis, providing estimates of gestation length, molar crown initiation, formation and completion times and minimum emergence ages for M1 and M2. Schwartz and colleagues find that molar development is rapid and poorly explained as a function of adult body mass. Microstructural indicators of dental development in a single female specimen of Pan paniscus are described by Ramirez-Rozzi and LaCruz. Preliminary results from the analysis of perikymata and striae counts reveal high appositional rates and short crown formation time for I1 while molar crown formation time is similar to that of the common chimpanzee.

New data on chimpanzee and human molar crown development are presented by Tanya Smith and associates, who document variation in incremental features within and between genera. Within cusp types humans show greater average cusp formation times than chimpanzees due either to thicker cuspal enamel and/or higher mean periodicity values. High variability in cusp formation times and overlapping ranges raise concerns for interpreting small samples. Enamel microstructure of Australopithecus africanus

is documented by Bromage and colleagues, who employed a portable confocal scanning optical microscope to circumvent analytic issues such as limited magnification and specimen preparation. Cross-striation periodicity and data on striae-EDJ angles are presented and crown formation time for a single molar (STW 284, M2) is estimated at between 3.0 and 3.2 years. In the final paper in this section, Guatelli-Steinberg and associates compare imbricational enamel growth in the anterior teeth of Neandertals and three modern human groups from diverse eco-geographic settings. While no significant difference was found in imbricational enamel formation times for anterior teeth, differences were evident in the shape of growth curves (from cusp tip to cervix) and in mean perikymata numbers across anterior tooth types.

Part III is devoted to 'Dental development' and consists of four chapters spanning dental genetics and tooth size, dental development sequences, inter-group variation in calcification stages and new methods for reconstructing dental ontogeny. Tooth size variation in outbred pedigreed populations of baboons and mice were used by Hlusko and Mahaney to test expectations derived from dental field theory. In mice, incisor size appears to be genetically independent of molar size, and circumstantial evidence from fossils suggests that some level of independence exists in the expression of anterior and post-canine tooth size in primates. Braga and Heuze introduce the concept of modularity to assess interactions between inter-dependent elements in growing dentitions. They observe considerably greater plasticity and variability in development timing of incisors than of other teeth and advise caution in using incisor teeth as a reliable substitute for other permanent teeth in the interpretation of fossils. Preliminary results from an on-going analysis of permanent molar calcification stages (M1 and M2) in African-American and European-American children are presented by Monge and associates, who find evidence of earlier maturation among children born in the 1990s. A re-evaluation of what constitutes 'normal' dental development and greater appreciation for the range of plasticity in dental calcification is encouraged.

Serial micro-CT scans are used by Smith and colleagues to reconstruct the topography of the dento-enamel junction and quantify cusp volume and relationships during successive stages of development. This research suggests that spatial relationships consist of shape differences that are established early in morphogenesis by differential development within the tooth germ, and that differences in cusp size and proportions are modified at the crown surface by enamel apposition.

Dental wear and elemental ratios in fossil hominin and modern human teeth are addressed by five diverse contributions to Part IV, entitled 'Dentition and diet". An innovative method known as laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) was used by Humphrey and colleagues to determine changes in Sr/Ca ratios across the neonatal line in deciduous teeth of formula-fed and breast-fed children. Marked reduction in Sr/Ca ratios were detected across the neonatal line in breast-fed children but not in formula-fed children, a result that holds promise for interpreting the chronology of dietary transitions in infancy and early childhood. Tooth crown topography, a landmark-free, 3D method of describing crown morphology, is employed by Ungar to show that differences in diet can be inferred from worn teeth in extant apes, that species-specific wear patterns allow inferences of function from form in worn teeth, and that differences in molar crown topography in Paranthropus and Australopithecus suggest differences in diet and fallback foods.

A retrospective review of past accomplishments and vision of future developments in the field of dental microwear is provided by Teaford, who regards 'low magnification' methods and scale-sensitive fractal analysis as 'next steps' in this rapidly developing field. Ulhaas and colleagues employ 3-D analysis of occlusal surface wear to comparatively assess variation in three hominin taxa: *A. afarensis*, *A. africanus*, and *Paranthropus robustus*. Using a portable optical triangulation scanner, inter-specific differences in the mode of reduction in occlusal relief was responsible for enhancing variation in wear facet orientation, an observation that implies low levels of interspecies competition for food. In the final chapter of the book, Estebaranz and associates use micrographs (SEM) and 3-D topographic images of molar buccal surfaces to characterize striation density and enamel surface roughness in three extant and three fossil hominin taxa. Postmortem surface damage and automated data acquisition were considered in this study which found a clear and significant association between some measures of enamel roughness and microwear pattern, a finding of value in inferring diet.

Overall, I found the volume a valuable review of emerging methods and new approaches to the use of dental morphology, microstructure, development, and wear in unraveling critical issues in human evolution. The hominin focus of the volume, made some chapters (Part II, chapter 2: lemur dental development; Part III, chapter 2: quantitative genetics of mice and monkeys) seem either out-of-place, or a refreshing departure from the main theme. The book is top-heavy with introductions (to the volume and then again to each individual section), yet lacking in summary, synthetic or integrative perspectives either by section, or for volume as a whole. This is an unfortunate omission. Though diverse in their objectives and methods, the contributions to this volume exhibit significant overlap in the questions posed and the results derived. A

comparative assessment of contributions, followed by a summary of the issues and themes that were consistently affirmed, as well as those on which divergent interpretations exist, would have been a valuable service to the reader.

As with many edited volumes, contributions are variable though in different ways; some chapters fail to yield definitive conclusions due to limitations of either sample size or methodology or both; while others present innovative and potentially useful analytical methods that suffer from operational complexity limiting their adoption by other investigators. Finally, it's sad that a volume devoted to cutting-edge technology contains so many annoying errors. For example, some text citations are missing from the References in the introduction to Part I (page 5, Martin-Torres *et al*., 2007; and Kono, 2004). Elsewhere (Part I, chapter 5), text references to illustrations are incorrect: a) on page 70, in discussing lower second premolar morphology, the reader is referred to Figure 3, which illustrates lower second molar occlusal surfaces. Again on page 73, in discussing molar cusp number, the reader is referred to Figure 5 which illustrates lower first premolar teeth. Sloppy editing, or inept use of the spell-checker, results in some awkward sentences; for example, on page 188, we read "... when discussing variation in enamel developmental, ..." and "In light if this, ...", and page 189, "... If is unclear why this population ...."

Researchers, teachers and graduate students in human and dental evolution, and possibly in allied clinical fields, will find the volume an indispensable and essential aid in keeping abreast of current developments in dental anthropology. However, given the rapid rate of change in method and theory in dental paleoanthropology, I'm concerned about the shelf-life of books devoted to cutting-edge issues and technology that require a significant financial investment.

John R. Lukacs
Department of Anthropology
University of Oregon, Eugene,
Oregon.E-mail: jrlukacs@oregon.
uoregon.edu

DAA Subscription

The secretary-treasurer of the **Dental Anthropology Association** is Dr. Loren R. Lease of Youngstown State University.

Dr. Loren R. Lease
Department of Sociology and Anthropology
Youngstown State University
One University Plaza
Youngstown, Ohio 44555 USA

Telephone: (330) 941-1686
E-mail: lrlease@ysu.edu

Dental Anthropology now is published electronically and e-mailed to all members as a PDF. The PDF is published with color illustrations, though the printed version is in black-and-white. If you **also** want to receive a hard copy, be sure to make this clear on the membership form at the DAA website or contact Loren.

Speed communication about your membership by contacting Loren directly (other officers may not have current membership lists).

Electronic versions (as PDF files) of the back issues of *Dental Anthropology* are available *gratis* at the Association's web site that is maintained at The Ohio State University: The web site's home page is:

http://anthropology.osu.edu/DAA/index.htm

NOTICE TO CONTRIBUTORS

Dental Anthropology publishes research articles, book reviews, announcements and notes and comments relevant to the membership of the *Dental Anthropology Association*. Editorials, opinion articles, and research questions are invited for the purpose of stimulating discussion and the transfer of information. Address correspondence to the Editor, Dr. Edward F. Harris, Department of Orthodontics, University of Tennessee, Memphis, TN 38163 USA (E-mail: eharris@utmem.edu). Electronic submissions are encouraged.

Research Articles. The manuscript should be in a uniform style (one font style, with the same 10- to 12-point font size throughout) and should consist of seven sections in this order:

Title page	Tables
Abstract	Figure Legends
Text	Figures
Literature Cited	

The manuscript should be double-spaced on one side of 8.5 x 11" paper (or the approximate local equivalent) with adequate margins. All pages should be numbered consecutively, beginning with the title page. Submit three (3) copies—the original and two copies—to the Editor at the address above (or see Electronic Submission, below). Be certain to include the full address of the corresponding author, including an E-mail address. All research articles are peer reviewed; the author may be asked to revise the paper to the satisfaction of the reviewers and the Editor. All communications appear in English.

Title Page. This page contains (a) title of the paper, (b) authors' names as they are to appear in publication, (c) full institutional affiliation of each author, (d) number of manuscript pages (including text, references, tables, and figures), and (3) an abbreviated title for the header. Be certain to include a working E-mail address and/or telephone number.

Abstract. The abstract does not contain subheadings, but should include succinct comments relating to these five areas: introduction, materials, methods, principal results, and conclusion. The abstract should not exceed 200 words. Use full sentences. The abstract has to stand alone without reference to the paper; avoid citations to the literature in the abstract.

Figures. One set of the original figures must be provided (or e-mailed) with the manuscript in publication-ready format. Drawings and graphics should be of high quality in black-and-white with strong contrast. Graphics on heavy-bodied paper or mounted on cardboard are encouraged; label each on the back with the author's name, figure number, and orientation. Generally it is preferable to also send graphs and figures as computer files that can be printed at high resolution (300 dpi or higher). Most common file formats (Windows or Macintosh) are acceptable; check with the Editor if there is a question. The hard-copy journal does not support color illustrations, but the PDF version does. Print each table on a separate page. Each table consists of (a) a table legend (at top) explaining as briefly as possible the contents of the table, (b) the table proper, and (c) any footnotes (at the bottom) needed to clarify contents of the table. Whenever possible, provide the disk-version of each table as a tab-delimited document; do not use the "make table" feature available with most word-processing programs. Use as few horizontal lines as possible and do *not* use vertical lines in a table.

Literature Cited. *Dental Anthropology* adheres strictly to the current citation format of the *American Journal of Physical Anthropology*. Refer to a current issue of the *AJPA* or to that association's web-site since the "current" style is periodically updated. Current guidelines are available at the AAPA website (http://www3.interscience.wiley.com/journal/28130/home). *Dental Anthropology* adheres to the in-text citation style used by the *AJPA* consisting of the author's last name followed by the year of publication. References are enclosed in parentheses, separated by a semicolon, and there is a comma before the date. Examples are (Black, 2000; Black and White, 2001; White *et al*., 2002). The list of authors is truncated and the Latin abbreviation "*et al*." is substituted when there are three or more authors (Brown *et al*., 2000). However, *all* authors of a reference are listed in the Literature Cited section at the end of the manuscript.

Electronic Submission. Electronic submission *instead of* sending hard copies of articles is strongly encouraged. For articles that undergo peer review, the editor will request submission of the final revision of a manuscript in electronic format, not interim versions. Files can be submitted on a 3.5" diskette, or a 100-megabyte Iomega Zip disk or a compact disk (CD), either in Windows or Macintosh format. **Files can also be sent as E-mail attachments**. Microsoft Word documents are preferred, but most common formats are suitable. Submit text and each table and figure as a separate file. Illustrations should be sent in PDF or EPS format, or check with the Editor before submitting other file types. Be certain to label any disk with your name, file format, and file names.

Dental Anthropology

Volume 22, Number 1, 2009

Original Articles

Book Review

Published at
Craniofacial Biology Laboratory, Department of Orthodontics
College of Dentistry, The Health Science Center
University of Tennessee, Memphis, TN 38163 U.S.A.