

DELAYED DENTAL DEVELOPMENT IN CHILDREN WITH ISOLATED CLEFT LIP AND PALATE

E. F. HARRIS and J. G. HULLINGS

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

(Accepted 24 November 1989)

Summary—Although most cases of cleft lip and palate are free of other developmental defects, children with isolated cleft lip/palate are at enhanced risk of delayed growth and reduced final size. Three variables were assessed in the permanent dentition away from the cleft site: congenital absence by tooth type (which ranged from 0 to 7%) asymmetry in developmental staging (3 times more common in cleft lip/palate than in controls), and dental age (with a mean delay of 0.9 yr in cleft lip/palate relative to controls). The pervasive nature of these measures of reduced growth potential and developmental control, which were greatest in teeth forming during infancy, suggests that the cause of the compromised growth is the adverse early postnatal environment rather than conditions intrinsic to the individual.

Key words: tooth formation, growth, hypodontia, bilateral asymmetry, cleft lip/palate.

INTRODUCTION

The overall incidence of cleft lip and palate is in the order of 3 per 1000 live births (Vanderas, 1987; Sayetta, Weinrich and Coston, 1989). The great majority of cases (85–90%) have no other developmental disorder but, as a group, these children are at risk for small size (Hunter and Dijkman, 1977; Cooper, Harding and Krogman, 1979; Jensen, Dahl and Kreiborg, 1985; Bowers *et al.*, 1987), slower growth (Menius, Largent and Vincent, 1966; Bailit, Doykos and Swanson, 1968; Ranta, 1984) and other postnatal deficiencies (Ross, 1965; Dahl, 1970; Ross and Johnston, 1972).

It may be that attenuated growth is a subtle consequence of the clefting disorder. Alternatively, as youngsters with cleft lip/palate are substantially more likely to experience feeding difficulties, contract upper respiratory infections and undergo repeated hospitalizations for lip and palate repairs, their delayed development may thus be a consequence of a debilitating postnatal environment (Cox, 1960; Ross, 1965; Drillien, Ingram and Wilkinson, 1966; Hunter and Dijkman, 1977). Whether attenuated growth is congenital or acquired, it is a common clinical perception that teeth of children with isolated cleft lip/palate are slower to form and to erupt.

To more fully assess the degree of dental involvement, we have now evaluated tooth formation in a group of children with isolated cleft lip/palate and contrasted this with a control group matched for race, sex and age.

MATERIALS AND METHODS

Orthopantomograms were taken of 54 children with isolated cleft lip/palate (35 unilateral, 19 bilateral) in preparation for orthodontic treatment. Mean age at examination was 9.5 yr (SD = 1.9). No child had a growth disorder aside from cleft lip/palate. All

subjects were caucasian and each was matched to a phenotypically normal subject of the same sex and chronological age (± 3 months).

The mineralization stage of each permanent tooth was scored with the grading scheme of Moorrees, Fanning and Hunt (1963). Incisors were, however, omitted as most had already completed root formation and because of variation in radiographic quality near the midline. Both left and right sides were scored to assess bilateral symmetry of development (Adams and Niswander, 1967; Garn, Lewis and Kerewsky, 1966). Congenitally absent teeth were noted but were not used in the determination of asymmetry of the estimation of dental age because hypodontia is a separate entity (Grahnen, 1956; Suarez and Spence, 1974).

Dental age was determined using the race- and sex-specific standards of Harris and McKee (1990), which are based on children from the same population as those with cleft lip/palate assessed here and, consequently, account for secular and regional differences in the tempo of growth. Each scorable tooth was assigned the median chronological age from the Harris-McKee standards for that formation stage. Both left and right teeth were scored, and the ages for the two sides were averaged; this yielded tooth-specific dental ages. Normative dental ages for all scorable teeth were also averaged for each subject to arrive at his or her overall dental age and compared to the individual's chronological age.

RESULTS

Congenital absence

Even though teeth at the cleft site were omitted, there was a considerable increase in hypodontia with cleft lip/palate that extended throughout the dentition (Table 1). Second premolars and third molars were most likely to be hypodont, both averaging 5%.

Table 1. Frequencies (%) of congenitally absent teeth in cleft lip/palate children and matched controls

Tooth*	Controls	Cleft lip/palate	p-Value†
MAXILLA			
C	0	0	1.00
P1	0	0	1.00
P2	0	6.5	0.01
M1	0	0	1.00
M2	0	3.7	0.06
M3	0	4.6	0.03
MANDIBLE			
C	0	2.8	0.12
P1	0	1.9	0.25
P2	0	4.6	0.03
M1	0	0	1.00
M2	0	3.7	0.06
M3	1.9	4.6	0.22

*Tooth abbreviations are canine (C), premolars (P), and molars (M).

Sample size is 108 (number of scorable quadrants) for all counts.

†From Fisher exact tests for differences in frequencies between groups.

There was little difference between the frequencies of hypodontia in the two arches although the overt defect was limited to the maxilla. There was no instance of congenital absence of the first molars, the only teeth in which mineralization begins before birth. Taken altogether, the odds ratio (Rosner, 1986) showed that the risk of a missing tooth was 17.9 times greater in the cleft lip/palate series.

Bilateral asymmetry

Genetic information is assumed to be the same across the two sides of the body; minor, random failures to achieve structural symmetry are attributed to localized insults (Adams and Niswander, 1967; Barden, 1980). Left-right differences in developmental staging were higher in the cleft lip/palate group for each of the 12 tooth types (Table 2). Asymmetries were highest for those teeth that also were most likely to be congenitally absent (P2, M3). Across all teeth, the odds ratio showed the cleft lip/palate series to be

at 3.0 times the risk of asymmetry in developmental staging.

Delayed formation

Tooth-specific assessments disclosed that the cleft lip/palate series had substantially delayed dental development, and there was considerable concordance between the maxillary and mandibular homologues (Spearman rank correlation, $r_s = 0.94$). It is noteworthy that there appeared to be a temporal gradient in the degree of involvement (Fig. 1). Teeth forming during the early postnatal period (C, M1) were most affected, while later forming elements were less delayed (P1, P2), and the teeth forming latest (M2, M3) were least affected. It also is likely that the delay in maxillary canine formation was attributable in part to being adjacent to the cleft site and, thereby, sharing in the localized growth distortions (Sofaer, 1979); this would not, however, explain the similar delay in formation of the mandibular canine.

Table 2. Frequencies of bilateral asymmetries in the staging of tooth formation in cleft lip/palate and matched controls

Tooth	Controls		Cleft lip/palate		p-Value*
	n	%	n	%	
MAXILLA					
C	54	0	53	13	0.01
P1	49	4	48	4	0.33
P2	52	2	44	20	0.00
M1	54	0	52	2	0.49
M2	52	2	52	6	0.31
M3	52	10	51	22	0.08
MANDIBLE					
C	50	0	52	4	0.26
P1	52	4	53	8	0.35
P2	54	9	50	18	0.15
M1	54	2	53	8	0.17
M2	54	6	52	10	0.34
M3	53	11	51	20	0.18
POOLED TOOTH COUNTS					
Maxilla	313	3	300	12	0.00
Mandible	317	5	311	11	0.01
All teeth	630	4	611	11	0.00

*Two-tail tests from likelihood-ratio chi-square.

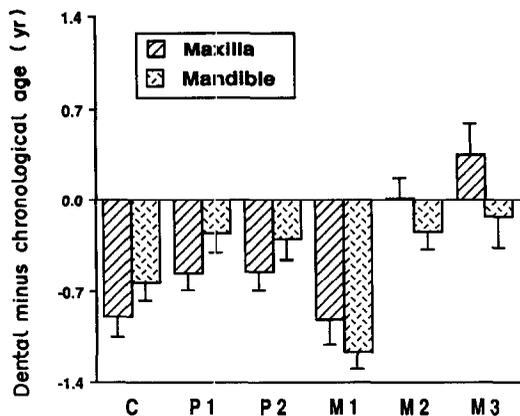


Fig. 1. Mean (\pm SE) differences between chronological and dental ages, by tooth.

Averaging across all scorable teeth (C through M3) yielded a mean delay of 0.9 yr (*ca* 11 months) relative to chronological age. The high prevalence of delayed dental age is illustrated in Fig. 2 where 89% (48/54) of the cases have dental ages less than their chronological ages.

DISCUSSION

It is well documented that teeth close to the cleft site, notably the lateral incisor, are likely to have various malformations (Böhn, 1963; Ranta, 1986). The important issue here is that hypodontia, bilateral asymmetry of developmental staging, and delayed development were not localized to the cleft defect; they were altered across all tooth types and throughout both dental arcades.

These dental sequelae yield valuable insights into the developmental processes of children with isolated cleft lip/palate. In conjunction with tooth crown size (Sofaer, 1979; Werner and Harris, 1989) and morphology (Jordan, Kraus and Neptune, 1966; Kraus, Jordan and Pruzansky, 1966), tooth formation constitutes a sensitive measure of overall health (Niswander, 1963; Bailit, 1975). It is informative that both stable (and earlier forming) and variable teeth within

each morphogenetic field were discernibly retarded. Of the 12 tooth types examined, only the first molars form and begin crown mineralization before birth, and these were the least affected teeth with regard to the three criteria assessed here. The canine also is notably stable by a number of measures (Dahlberg, 1945; Garn, Osborne and McCabe, 1979), but, presumably because of its later, postnatal formation, it was distinctly affected in cleft lip/palate. In contrast, Böhn has shown that deciduous (prenatally forming) teeth outside the cleft site are only as variable as those of controls. So too, prenatal development of the primary teeth in cleft palate appears to start and proceed at the same rate as in non-cleft controls (Pöyry and Ranta, 1986) and eruption times are minimally affected by the cleft (Pöyry and Ranta, 1985). Observed differences seem trivial given the variability of some samples (subjects with isolated clefts combined with those exhibiting multiple anomalies), pooled sexes and the need to correct for increased prematurity and low birth weights in the cleft samples (Rintala and Gylling, 1967; Avedian and Ruberg, 1980; Seow, Humphreys and Tudehope, 1987; Angelos *et al.*, 1989).

Ranta (1984) has estimated the delay in dental formation to be on the order of 0.7 yr (8.4 months) in children with cleft palate. This is in close agreement with the mean delay of 0.9 yr that we found, particularly given the variability inherent in the sorts of clefts examined, the choice of a reference population and the method of analysis (Dahlberg and Menegaz-Bock, 1958).

As suggested here and in several previous studies, there is actually a collage of concurrent and interrelated features in cleft lip/palate just as in a variety of other craniofacial anomalies. These include (1) deviant (generally slower) growth tempo, assumed to be due to lower mitotic rates (e.g. Curé, Boué and Boué, 1974; Nielsen, Marcus and Gropp, 1985), (2) reduced tooth size (e.g. Foster and Lavelle, 1971), (3) increased variability in size and growth tempo, including higher prevalences of missing and malformed elements (Olin, 1964; Dixon, 1966; Fishman, 1970), (4) increased bilateral asymmetry (Ranta, 1973), and (5) decreased integration (lowered covariation) among organ and tissue systems (Olson and Miller, 1958; Shapiro, 1970).

It is common to view these findings in light of the parallel models of reduced canalization (Waddington, 1942) and diminished developmental homeostasis (Lerner, 1954). The implication is that the impaired genotype is less capable of maintaining the proper track in the developmental pathway from conception to maturity. In genetic and chromosomal anomalies (of which some cleft lip/palate cases are the result) this is likely to be the case. On the other hand, in the majority of individuals with cleft lip/palate the defect is sporadic and the genetic contribution is less clearly defined. In this subset of isolated cleft cases it is arguable that, rather than a diminished growth potential, the immediate cause of the slowed growth tempo and smaller size is the more severe postnatal environment. Recurrent upper respiratory infections, middle ear infections, sequential surgical bouts and feeding problems, in addition to the psychosocial impact of the cleft, may well account for the ob-

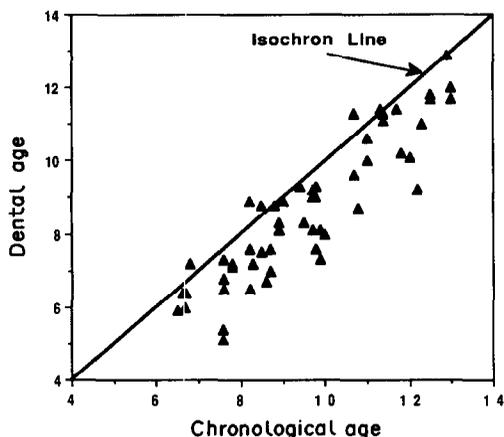


Fig. 2. Scatter plot of the observed dental versus the chronological (expected) ages of the 54 cleft lip/palate cases.

served delays with no need to invoke intrinsic mechanisms.

Of course, this scenario does not hold for cleft lip/palate in the broad sense because of the multiple aetiologies involved (Fraser, 1971). On a case-by-case basis, one is hard pressed to suggest a certain aetiology for the great bulk of cases (Smith, 1982). What we are suggesting is that the observed permanent tooth dysmorphologies (absence, retardation, asymmetry) away from the cleft and throughout both arches argue for the postnatal environment being generally more adverse for the cleft lip/palate infant. If the insult were temporally localized and tied to the clefting defect during palatogenesis, the distribution of dental defects would be far more localized within the permanent dentition and would preferentially affect the deciduous teeth. Neither of these conditions actually occurs.

REFERENCES

- Adams M. S. and Niswander J. D. (1967) Developmental 'noise' and a congenital malformation. *Genet. Res.* **10**, 313-317.
- Angelos G. M., Smith D. R., Jorgenson R. and Sweeney E. A. (1989) Oral complications associated with neonatal oral tracheal intubation: a critical review. *Pediat. Dent.* **11**, 133-140.
- Avedian L. V. and Ruberg R. L. (1980) Impaired weight gain in cleft palate infants. *Cleft Palate J.* **17**, 24-26.
- Bailit H. L. (1975) Dental variation among populations: an anthropologic view. *Dent. Clin. N. Am.* **19**, 125-139.
- Bailit H. L., Doykos J. D. and Swanson L. T. (1968) Dental development in children with cleft palate. *J. dent. Res.* **47**, 668.
- Barden H. S. (1980) Fluctuating dental asymmetry: a measure of developmental instability in Down syndrome. *Am. J. phys. Anthrop.* **52**, 169-73.
- Böhn A. (1963) Dental anomalies in harelip and cleft palate. *Acta odont. scand. Suppl.* **38**, 1-109.
- Bowers E. J., Mayro R. F., Whitaker L. A., Pasquariello P. S., LaRossa D. and Randall P. (1987) General body growth in children with clefts of the lip, palate and craniofacial structures. *Scand. J. Plast. Reconstr. Surg.* **21**, 7-14.
- Cooper H. K., Harding R. L. and Krogman W. M. (Eds) (1979) *Cleft Palate and Cleft Lip: A Team Approach to Clinical Management and Rehabilitation of the Patient*. Saunders, Philadelphia, PA.
- Cox M. A. (Ed.) (1960) *Toronto Research Institute, the Cleft Lip and Palate Treatment Centre: A Five Year Report, 1955-1959*. Hospital for Sick Children, Toronto.
- Curé S., Boué J. and Boué A. (1974) Growth characteristics of human embryonic cell lines with chromosomal anomalies. *Biomedicine* **21**, 233-236.
- Dahl E. (1970) Craniofacial morphology in congenital clefts of the lip and palate. *Acta odont. scand. Suppl.* **57** **28**, 13-165.
- Dahlberg A. A. (1945) The changing dentition of man. *J. Am. dent. Ass.* **32**, 676-690.
- Dahlberg A. A. and Menegaz-Bock R. (1958) Emergence of the permanent teeth in Pima Indian children: a critical analysis of methods and an estimate of population parameters. *J. dent. Res.* **37**, 1123-1140.
- Dixon D. A. (1966) Abnormalities of the teeth and supporting structures in children with clefts of lip and palate. In: *The Causes and Natural History of Cleft Lip and Palate* (Edited by Drillien C. M., Ingram T. T. S. and Wilkinson E. M.) pp. 178-183. Livingstone, London.
- Drillien C. M., Ingram T. T. S. and Wilkinson E. M. (1966) *The Causes and Natural History of Cleft Lip and Palate*. Livingstone, London.
- Fishman L. S. (1970) Factors related to tooth number, eruption time, and tooth position in cleft palate individuals. *Cleft Palate J.* **8**, 177-184.
- Foster T. D. and Lavelle C. L. B. (1971) The size of the dentition in complete cleft lip and palate. *Cleft Palate J.* **8**, 177-184.
- Fraser F. C. (1971) Etiology of cleft lip and palate. In: *Cleft Lip and Palate: Surgical, Dental, and Speech Aspects* (Edited by Grabb W. C., Rosenstein S. W. and Zoch K. R.) pp. 54-65. Little, Brown, Boston, MA.
- Garn S. M., Lewis A. B. and Kerewsky R. S. (1966) The meaning of bilateral asymmetry in the permanent dentition. *Angle Orthod.* **36**, 55-62.
- Garn S. M., Osborne R. H. and McCabe K. D. (1979) The effect of prenatal factors on crown dimensions. *Am. J. phys. Anthrop.* **51**, 665-678.
- Grahnen H. (1956) Hypodontia in the permanent dentition: a clinical and genetical investigation. *Odont. Revy Suppl.* **3**, 1-100.
- Harris E. F. and McKee J. H. (1990) Tooth mineralization standards for blacks and whites from the Midsouth United States. *J. Forensic Sci.* In press.
- Hunter W. S. and Dijkman D. J. (1977) The timing of height and weight deficits in twins discordant for cleft of the lip and/or palate. *Cleft Palate J.* **14**, 158-166.
- Jensen B. L., Dahl E. and Kreiborg S. (1983) Longitudinal study of body height, radius length and skeletal maturity in Danish boys with cleft lip and palate. *Scand. J. dent. Res.* **91**, 473-481.
- Jordan R. E., Kraus B. S. and Neptune C. M. (1966) Dental abnormalities associated with cleft lip and/or palate. *Cleft Palate J.* **3**, 22-55.
- Kraus B. S., Jordan R. E. and Pruzansky S. (1966) Dental abnormalities in the deciduous and permanent dentitions of individuals with cleft lip and palate. *J. dent. Res.* **5**, 1736-1746.
- Lerner I. M. (1954) *Genetic Homeostasis*. Oliver & Boyd, London.
- Menius J. A., Largent M. D. and Vincent C. J. (1966) Skeletal development of cleft palate children as determined by hand-wrist roentgenographs, a preliminary study. *Cleft Palate J.* **3**, 67-75.
- Moorrees C. F. A., Fanning E. A. and Hunt E. E. Jr (1963) Age variation of formation stages for ten permanent teeth. *J. dent. Res.* **42**, 1490-1502.
- Nielsen K., Marcus M. and Gropp A. (1985) *In vitro* growth kinetics of mouse trisomies 12 and 19. *Hereditas* **102**, 77-84.
- Niswander J. D. (1963) Effects of heredity and environment on development of dentition. *J. dent. Res.* **42**, 1288-1296.
- Olin W. H. (1964) Dental anomalies in cleft lip and palate patients. *Angle Orthod.* **34**, 119-123.
- Olson E. C. and Miller R. L. (1958) *Morphological Integration*. University of Chicago Press, Chicago, IL.
- Pöyry M. and Ranta R. (1985) Emergence of deciduous teeth in children with oral clefts. *Proc. Finn. dent. Soc.* **81**, 171-176.
- Pöyry M. and Ranta R. (1986) Formation of anterior maxillary teeth in 0-3-year-old children with cleft lip and palate and prenatal risk factors for delayed development. *J. Craniofac. Genet. Devl Biol.* **6**, 15-26.
- Ranta R. (1973) Asymmetric tooth formation in the permanent dentition of cleft-affected children. *Scand. J. Plast. Reconstr. Surg.* **7**, 59-63.
- Ranta R. (1984) Associations of some variables to tooth formation in children with isolated cleft palate. *Scand. J. dent. Res.* **92**, 496-502.
- Ranta R. (1986) A review of tooth formation in children with cleft lip/palate. *Am. J. Orthod. Dentofac. Orthop.* **90**, 11-18.

- Rintala A. E. and Gylling U. (1967) Birth weight of infants with cleft lip and palate. *Scand. J. Plast. Reconstr. Surg.* **1**, 109-112.
- Rosner B. (1986) *Fundamentals of Biostatistics*, 2nd edn. Duxbury Press, Boston, MA.
- Ross R. B. (1965) Cranial base in children with lip and palate clefts. *Cleft Palate J.* **2**, 157-166.
- Ross R. B. and Johnston M. C. (1972) *Cleft Lip and Palate*. Williams & Wilkins, Baltimore, MD.
- Sayetta R. B., Weinrich M. C. and Coston G. N. (1989) Incidence and prevalence of cleft lip and palate: What we think we know. *Cleft Palate J.* **26**, 242-248.
- Seow W. K., Humphreys C. and Tudehope D. I. (1987) Increased prevalence of developmental dental defects in low birth-weight, prematurely born children: a controlled study. *Pediat. Dent.* **9**, 221-225.
- Shapiro B. L. (1970) Prenatal dental anomalies in mongolism: comments on the basis and implications of variability. *Ann. N.Y. Acad. Sci.* **171**, 562-577.
- Smith D. W. (1982) *Recognizable Patterns of Human Malformations: Genetic, Embryologic and Clinic Aspects*, 3rd edn. Saunders, Philadelphia, PA.
- Sofaer J. A. (1979) Human tooth size asymmetry in cleft lip with or without cleft palate. *Archs oral Biol.* **24**, 141-146.
- Suarez B. K. and Spence M. A. (1974) The genetics of hypodontia. *J. dent. Res.* **53**, 781-785.
- Vanderas A. P. (1987) Incidence of cleft lip, palate, and cleft lip and palate among races: a review. *Cleft Palate J.* **24**, 216-225.
- Waddington C. H. (1942) The canalization of development and the inheritance of acquired characters. *Nature* **150**, 563-565.
- Werner S. P. and Harris E. F. (1989) Odontometrics of the permanent teeth in cleft lip and palate: systemic size reduction and amplified fluctuating asymmetry. *Cleft Palate J.* **26**, 36-41.