
SZEGED
2007
FOGORVOSTUDOMÁNYI KAR

Seregek jönnek Hozzád megköszönni,
Fejedelem, a százados csodát,
hogy milliónyi magrejtő rögödből
virtust nevelt „vitézlő oskolád.”

Áprily Lajos: A Fejedelemhez

Édesapám,
Prof. Dr. Dipl. Ing. RÓZSA FERENC,
A Nagyenyedi Bethlen Kollégium kiváló diákja,
A Bukaresti Műszaki Egyetem Építészeti Karának
Tanszékvezető egyetemi tanára,
Emlékére

PH. D. Thesis

Prevalence and treatment possibilities of numerical, morphological dental anomalies and malposition during childhood

Dr. RÓZSA Noémi Katinka

UNIVERSITY OF SZEGED
Faculty of Dentistry
Graduate School of Clinical Science
Research in Dental Medicine

Head of the Program: Prof. Dr. Attila Dobozy,
Member of the Hungarian Academy of Science

Head of theDental Program : Prof. Dr. Zoltán Rakonczay PhD, DSc.

Coordinators: Prof. Dr. med habil Katalin Nagy, PhD
Prof. Dr. med habil Zoltán Vajó. PhD

Szeged, 2008

PUBLICATIONS RELATED TO THE THESIS

Journal articles:

I. **Gábris K, Tarján I, Csíki P, Konrád F, Szádeczky B, *Rózsa N*. *A maradó fogak csírahiányának előfordulási gyakorisága és a kezelés lehetőségei.*** Fogorv.Szle. 94. 137. 2001.

II. **Tarján I, *Rózsa N*, Tanikawa Y, Wakamatsu N, Tanase S. *The influx of serum albumin to enamel matrix in rat incisors after trauma.*** Calcified Tissue Int, 2002; 71:349-355, **IF: 2,053**

III. ***Rózsa N*, Fábián G, Szádecky B, ifj. Kaán M, Gábris K és Tarján I. *Retineált felső maradó szemfogak előfordulási gyakorisága és a kezelés lehetőségei 11-18 éves orthodonciai betegeken.*** Fogorv.Szle. 96. 65. 2003.

IV. **Tarján I, Gábris K, *Rózsa N*. *Early prosthetic treatment of patients with ectodermal dysplasia: A clinical report.*** J Prosthet Dent 2005; 93:419-424, **IF: 0,748**

V. **Tarján I, Gyulai-Gaál Sz, Soós A, *Rózsa N.* *Tuberculate and Odontoma Type Supernumerary Teeth.*** J Craniofac Surg 2005; 16(69):1098-1102, **IF:0,827**

VI. **Gábris K, Fábián G, Kaán M, *Rózsa N*, Tarján I. *Prevalence of hypodontia and hyperdontia in paedodontic and orthodontic patients in Budapest.*** Comm Dent Health 2006; 23:80-82

VII. **Mavrodisz K, *Rózsa N*, Budai M, Soós A, Pap I, Tarján I. *Prevalence of accessory tooth cusps in a contemporary and ancestral Hungarian population.*** Eur J Orthod 2007; 29:166-169, **IF: 0,651**

VIII. **Vajó Z, Kosa L, Szilvasy I, Pauliny Z, Bartha K, Visontay I, Kis A, Tarján I, *Rózsa N*, Jankovics I. *Safety and Immunogenicity of a Prepandemic Influenza A (H5N1) Vaccine in Children.*** Pediatr Infect Dis J. 2008 Oct 30. [Epub ahead of print] PMID: 18978514.

IX. ***Rózsa N*, Nagy K, Vajó Z, Gábris K, Soós A, Albert M, Tarján I.*.*Prevalence and distribution of permanent canine agenesis in paedodontic and orthodontic patients in Hungary.*** Unpublished results, Eur J Orthod 2008, under revision, considered for publication.

Meeting abstracts, posters, presentations:

1. **Tanase S, Tarján I, *Rózsa N,* Tanikawa Y, Wakamatsu N. *Effect of Experimentally Induced Trauma to incisors in rats.*** MFE XIII. Gyermekfogászati és Fogszabályozási Konferencia, Visegrád, 1994.
2. **Tanikawa Y, Tarján I, *Rózsa N*, Tanase S. *Effect of Experimentally Induced Trauma to incisors in rats.*** Abstract 50. XV. IAPD Congress, Göteborg, Sweden, 1995.
3. **Gábris K, Tarján I, *Rózsa N*, Frang E, Konrád F. *A maradó fogak számbeli rendellenességei és a kezelés lehetőségei.*** MFE XV. Gyermekfogászati és Fogszabályozási Konferencia, Dobogokő, 1999.
4. ***Rózsa N*, Mavrodisz K, Budai M, Soós A, Pap I, Tarján I. *Számfeletti csücskök előfordulási gyakorisága Árpád-kori koponyákon és napjainkban.*** Tudományos Továbbképző Konferencia és Fogorvostalálkozó, SZTE Tanulmányi és Információs Központ, Szeged 2007, április 20-22.

Table of contents

1.1. Introduction

Developmental dental anomalies are an important category of dental symptomatology. Their incidence and degree of expression can provide important information for phylogenic and genetic studies and help the understanding of variations within and among populations.

The prevalence studies of the present work were evaluations of young patient groups of different ages who presented for paedodontic and/or orthodontic treatment at the Department for Paedodontics and Orthodontics, Semmelweis University Budapest. Chi-square tests were used for statistical analysis.

1.1.1. Accessory cusps: Carabelli and talon cusps

Among the dental morphological characteristics the Carabelli and talon cusps are expressed in several degrees and different frequencies between humans, thus being useful to understand variations within and among species (Palonimo *et al.* 1977). A Carabelli cusp is a characteristic morphological developmental anomaly located on the mesial palatal surface of the upper first permanent molars. It is rarely present on the second or third permanent molars, or on the upper first primary molars. It has most commonly been detected symmetrically on both sides of the upper jaw (Alvesalo *et al*. 1975). The aetiology of the Carabelli cusp remains unknown. Both genetic and exogenous factors have been proposed. Most studies agree that the phenotypical appearance of the cusp is genetically determined (Dietz 1994). It was first described in 1842 by Carabelli (Mitchell 1892). According to Dahlberg (1963), there has been an evolution in the cusp form, from a simple groove to a well-developed cusp. It can be present with other atavistic traits like the Bolk cusp situated on the mesio-labial surface of the second and third upper permanent molars (Firu 1983).

A talon cusp is an uncommon characteristic morphological developmental anomaly referring to an accessory cusp like structure projecting from the cingulum area or cementoenamel junction of the maxillary or mandibular anterior teeth in both the primary and permanent dentitions (Hattab *et al*. 1996). The aetiology of talon cusp is also unknown. It has been suggested that this anomaly is primarily polygenetic with some environmental influence. The prevalence is higher in oriental races and it can be present with other syndromes, i.e. pin-shaped teeth, retained canines and odontomes (Davis and Rook 1985, Hattab *et al*. 1996, Henderson 1997, McNamara *et al*. 1998, Hedge and Kumar 1999). Mitchell (1892) first described the cusp, and Mellor and Ripa (1970) named the accessory cusp as ‘talon /claw/ cusp’ because of its resemblance in shape to an eagle’s talon.

1.1.2. Numerical dental anomalies:

1.1.2.1. Hyperdontia

Supernumerary teeth or hyperdontia are defined as the presence of accessory teeth, teeth which are additional to the normal compliment. They can occur in both, primary and permanent dentitions. The prevalence in permanent dentition is between 0.1 and 3.8% (McKibben and Brearly 1971, Brook 1984, Mitchell and Mitchell 1992, Stelzig *et al.* 1997) and may be part of developmental disorders.

Some authors (Babu *et al.* 1998, Gallass and Garcia 2000) suggested that the origin of hyperdontia could be partly hereditary or that similar dental anomalies such as hyperdontia, hypodontia, cleft lip and palate have a common genetic background. Hereditary tendencies were shown also for mesiodens (Stellzig *et al.* 1997, Baccetti 1998).

Supernumerary teeth can be classified according to morphology: conical, tuberculate, and supplemental and odontoma. They can also be categorized into three types according to location: mesiodens, paramolar and distomolar (Brook 1984, Garvey *et al.*1999). They may occur singly, in multiples; unilaterally or bilaterally in the maxilla, in the mandible, or both (Levine 1961, So 1990). Multiple supernumerary teeth can be found in syndromes such as Gardner's syndrome (Duncan *et al.* 1968), cleidocranial dysostosis (Richardson and Deussen 1994), Nance-Horan syndrome and cleft lip and palate, and less common developmental disorders, like Ehlers-Danlos syndrome (Melamed 1994). Supernumerary teeth especially in the maxillary anterior region can cause clinical problems: failure of eruption, displacement or rotation, crowding, etc. (Di Biase 1969, Hattab *et al.* 1994) and these indicate why the early treatment of this anomaly is recommended (Cozza *et al.* 2002, Munns, 1981).

1.1.2.2. Hypodontia

Considering the evolutionary perspective, the congenital absence (agenesio dentis) of one or more teeth is not uncommon in the modern human stomatognatic system. This tendency, in regard to reduction in tooth number, is believed to continue (Silverman and Ackerman, 1979). To allow uniform analysis Burzynski and Escobar (1983) suggested a trimodal classification of numeric teeth anomalies: anodontia, hypodontia, and oligodontia, and, further, a subclassification into nonsyndromic and syndromic cases.

The prevalence of hypodontia in permanent dentition reveals great variations between populations. Recent reports concerning the Caucasian population recorded prevalence between 3.9% and 11.3% (Larmour *et al.* 2005).

According to Bolk's theory of terminal reduction (de Beer, 1951) due to the phylogenetic evolution of mankind, the reduction of the distal element of a tooth-group occurs most frequently (Gábris *et al.* 2001, 2006, Muller *et al.* 1970, Brook 1984). Congenitally missing teeth (CMT) can occur in association with head and neck syndromes (Schalk van der Weide *et*

al. 1994) or under an isolated, nonsyndromic form (Burzynski and Escobar 1983, Fekonja 2005).

1.1.2.3. Congenitally missing permanent canines

Often in syndromic oligodontia, permanent canines are reported missing although with low frequency (Lombardo *et al.* 2007). Nonsyndromic permanent canines agenesis (PCA) or combined with hypodontia or congenitally missing of other tooth-types has been occasionally described in literature (Endo *et al.)*, but isolated forms are rarely mentioned (Altug-Atac 2007, Cho 2004, Cho and Lee 2004, Cho *et al.* 2004, Lombardo *et al.* 2007, Hallet and Weyman 1954, Lum and Lim 1976, Robertson 1962, Ulrich, 1989).

Some isolated cases of congenitally missing permanent canines were published earlier in the Hungarian population (Bakody 1974, 1975, Bótyik *et al.* 1977, László 1978, Bakody and Balaton 1992), but there are no available data on prevalence and distribution of PCA.

1.1.3. Malpositions: Impacted upper permanent canines

Impaction of upper permanent canines is the second most frequent tooth malposition form, it occurs in 1-2% of the population (Thilander and Jakobsson 1968, Rayne 1969, Richardson and Russel 2000). The exact aetiology of impacted maxillary canines is a controverse subject in the literature. Two theories focus on this common phenomenon: the genetic theory and "guidance theory of palatal canine displacement". The first theory proposes a genetic cause for this anomaly. Impacted maxillary canines often present with other developmental tooth anomalies like: numerical, morphological and structural abnormalities, all supposed to be genetically linked (Zilberman *et al.* 1990, Bacetti 1998). The "guidance theory of palatal canine displacement" is based on the fact that upper canines are among the last teeth to develop high in the upper jaw and their eruptional pathway is long and difficult (Ericson and Kurol 1986). So, a various number of local predisposing causes including congenitally missing lateral incisors, supernumerary teeth, odontomas, transposition of teeth and other mechanical factors can interfere with the canine eruption path (Thilander and Jakobsson 1968, Bacetti 1998, Richardson and Russel 2000).

Permanent upper canines are determinant elements of functional occlusion and aesthetics (Bishara 1992). Thus, any interference during their development and eruption can increase the risk of infection, follicular cyst formation and root resorption of neighbouring lateral incisors Rayne 1969, Power and Short 1993, Richardson and Russel 2000). If identified early, in specific cases, treatment choice is extraction of the persisting maxillary primary canines and/or permanent upper first premolars, followed by guided eruption and, eventually space

maintainer placement. This allows the correction of the canine eruption paths, and the impacted teeth will erupt in relatively good alignment (Ericson and Kurol 1988).

1.2. Goals

I. Our first aim was to determine the prevalence and degree of expression of both Carabelli and talon cusps in the contemporary Hungarian population and to evaluate their appearance from an anthropological point of view by comparison with the prevalence of these two dental characteristics on teeth from 11th century skulls.

II. Our second goal was to determine the prevalence of numerical dental anomalies such as hyperdontia and hypodontia in 6- to 18-year-old orthodontic patients in Hungary.

III. Our aim was also to determine the prevalence of congenitally missing permanent canines in 6- to 18-year-old orthodontic and paedodontic patients in Hungary.

IV. Further, the goal was to evaluate the prevalence of impacted upper permanent canine for orthodontic patients aged 11 to 18 years and to evaluate the principal treatment choices.

VI. Our final goal was to present treatment possibilities for patients with special form of tooth abnormities, such as tuberculate and odontoma type supernumerary teeth, talon cusps, permanent canine malposition and agenesis, and early treatment possibilities for hypodontia in patients with ectodermal dysplasia (ED).

2.Materials and Methods

2.1. Accessory cusps

The models of 600 children aged 7-18 years (average age 12 years), 304 males, 296 females, from the Department for Paedodontics and Orthodontics, Semmelweis University Budapest. and a total of 147 skulls from the Department of Anthropology of the Hungarian Natural History Museum dating from the 11^{tth} century were examined to determine the prevalence and distribution of Carabelli and talon accessory cusps on permanent dentition in contemporary and ancestral Hungarian population. The skulls were in a well preserved condition, with all maxillary teeth present. They were found in the Halimba-Cseres cemetery which consisted of 932 graves from the so-called Árpád-era (Török 1962). A chi-square test was used for statistical analysis.

Carabelli cusps were examined according to Dahlberg's scale. This classification divides the accessory cusps in seven types, according to their size (Table 2.1.1.) (Boros 1961, Dahlberg 1963).

The system used to determine talon cusps was developed by Hattab *et al.* (1996). According to this classification, talon cusps are divided into three types considering their shape and size (Table 2.1.2).

Table 2.1.1. *Dahlberg's scale for determination of degree and expression of Carabelli cusps*

0	No vertical ridges, pits, or other manifestations on the mesiolingual cusp;
1	Small vertical ridge and groove;
2	Small pit with minor grooves diverging from a depression;
3	Double vertical ridges or slight and incomplete cusp outline;
4	Y shape: moderate grooves curving in opposite directions;
5	Small tubercle;
6	Broad cusp outline or moderate tubercle;
7	Large tubercle with free apex in contact with lingual groove (height often approximates that of major cusps).

Table 2.1.2. *Classification of talon cusp using the scale of Hattab et al.(1996)*

Type 1	A defined cusp on the palatal surface of the incisors, it covers at least half of the distance between the incisal edge and the cementoenamel junction (CEJ);
Type 2	The cusp covers less than half of the distance between the incisal edge and the CEJ but it is larger than 1 mm;
Type 3	A small tuber located on the gingival third of the tooth. It can be T, Y or V shaped.

2.2 Numerical dental anomalies:

2.2.1. Hyperdontia and hypodontia

The OPGs of 2219 6- to 18-year-old orthodontic patients (1293 female and 926 male) were examined for evidence of hyperdontia and hypodontia. Patients with hypodontia were examined and medical history was taken to exclude the possibility that the missing teeth had been extracted or traumatically avulsed. Children with systemic diseases were excluded from the survey. In view of the age range of the studied population group and in accordance with current research practice, the congenitally absence of third molars was not included in the evaluated data. Chi-square test was used for statistical analysis.

2.2.2. Congenitally missing permanent canines

The OPGs and the medical history data of 4417 6- to 18-year-old children, with an average age of 11 years, male-to female ratio 1:1, were examined. Patients with systemic disease were excluded from the survey. The radiographs were studied for evidence of permanent canine agenesis and other associated developmental dental anomalies. Permanent teeth were identified as congenitally missing when there was no evidence in the records that they had

been extracted and when there was no sign of mineralization of the tooth crown on the OPGs (Endo *et al.,* 2006; Aasheim and Ogaard, 1993). Clinical and radiological diagnosis of hypodontia in permanent dentition is recommended to be made after the age of 6 with the exception of the third molar (Pirinen and Thesleff, 1995). For each case of cuspid agenesis a detailed dental history was obtained from the parents to exclude any possibility of the missing canines had been extracted or traumatically avulsed. The relatives (parents and/or siblings) were questioned also about family history of hypodontia. For each radiograph showing PCA, persistent primary canines, if present, were examined for the degree of root resorption and recorded.

2.3. Impacted upper permanent canines

The dental records and OPGs of 1858 patients (1120 female and 756 male), aged 11 to 18 years (average age was 12 years), were analysed. Patients suffering of systemic disease were excluded from the study. The study group was examined for unilateral or bilateral upper permanent canine retention. The presence of persisting primary canines was also considered. For the patients with canine impaction treatment was followed and registered.

Data were processed by means of the Statistical Package for Social Sciences (SPSS), version 10.0. Chi-square tests were conducted to examine the statistical significance at a level of 0.05.

3. Results

3.1. Accessory cusps

3.1.1. Carabelli cusps

The examination of the models of 600 orthodontic patients revealed 393 cases of Carabelli cusp on the upper first permanent molars. Prevalence was 65.34%. Of the 147 examined skulls, 51 presented Carabelli cusp, prevalence was 34% (Table 3.1.1.1). The difference between the contemporary group and the skulls of the Árpád-era was significant ($p<0.01$).

Table 3.1.1.1. *Distribution and prevalence of Carabelli and talon cusps on the contemporary study group and on 11th century skulls*

	Total patients	**Carabelli ***	**%**	**Talon****	**%**
Contemporary group	600	393	65.34	9	2.5
11th century skulls	147	206	34.00	6	40.8

* $p<0.01$; ** $p<0.001$

According to the Dahlberg's scale, in the contemporary group the prevalence of the smallest cusp was 11.3% and that of the largest cusp was 3.6%. The prevalence of the smallest and that of the largest cusp in the 11th century skulls was 11.7% (Table 3.1.1.2.).

Table 3.1.1.2. *Degree and expression of a Carabelli cusp in the contemporary patient group and 11th century skulls according to the scale of Dahlberg (1963)*

Dahlberg's scale	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Contemporary group	207	68	26	102	45	99	31	22
%	34.6	11.3	4.3	16.8	7.6	16.5	5.3	3.6
11th century skulls	6	9	12	5	5	3	5	6
%	11.7	17.6	23.5	9.8	9.8	5.88	9.8	11.7

The prevalence of Carabelli cusps "positive" presence (Dahlberg's scale 5, 6 and 7) was 25.40% for the contemporary group, and 9.52% for the skulls of the Árpád-era.

3.1.2. Talon cusps

Talon cusps were found in 15 subjects in the present-day population, prevalence 2.5%, and in 60 of the examined 11th century skulls, prevalence 40.8%. The difference in the number of talon cusps between the contemporary group and the Árpád-era skulls was significant ($p<0,001$). Twelve talon cusps in the contemporary group were type 1, two were type 2, and one type 3, all located on the upper lateral incisors. In two cases, the talon cusps were T shaped, and the rest were V shaped. For the skull-group 31 were type 1, 21 were type 2, and 8 were type 3 (Table 3.1.2.1). All were V shaped and located on the upper lateral incisors.

Table 3.1.2.1. *The prevalence and type of talon cusps in the contemporary and 11th century skulls according to the scale of Hattab et al. (1996)*

Talon cusps	**Total***	**Type 1**	**Type 2**	**Type3**
Contemporary group	15	12	2	1
%	2.5	2.00	0.33	0.16
11th century skulls	60	31	21	8
%	40.8	50.00	35.00	13.33

$p<0.001$

3.2. Numerical dental anomalies

3.2.1. Hyperdontia

The OPGs of the 2219 orthodontic patients revealed a total of 34 cases of hyperdontia presenting a total of 40 permanent supernumerary teeth: 28 cases with one each, and 6 cases with two each. The recorded prevalence of hyperdontia was 1.53% (Table 3.2.1.1).

Table 3.2.1.1. *Prevalence of hyperdontia and hypodontia*

	Total number of patients	%	Female patients	%	Male patients	%
Hyperdontia*	34	1.53	17	1.31	17	1.84
Hypodontia*	326	14.69	191	14.77	135	14.58

* $p < 0.05$;

77.50% of the accessory teeth were situated in the upper jaw and 97.50% of the accessory teeth were in the anterior region. Distribution of accessory teeth in the upper jaw is shown in Table 3.2.1.2, and that in the lower jaw in Table 3.2.1.3.

Table 3.2.1.2.. *Distribution of accessory teeth in the upper jaw*

Accessory tooth type	Nr.	%
Mesiodens	13	32.5
Supplemental lateral incisor	9	22.5
Supplemental first incisor	6	15.0
Supernumerary tooth in the anterior area	2	5.0
Supplemental premolar	1	2.5
Total upper accessory teeth	31	77.5

Table 3.2.1.3. *Distribution of accessory teeth in the lower jaw*

Accessory tooth type	Nr.	%
Supernumerary tooth in the anterior area	6	15.0
Supplemental incisor	3	7.5
Total lower accessory teeth	9	22.5

3.2.2. Hypodontia

Table 3.2.2.1. *Prevalence of hypodontia according to tooth type*

Congenitally missing germ	Nr. of patients	%
Upper lateral incisor	73	3.29
Total second premolar	95	4.28
Lower second premolar	45	2.02
Upper second premolar	12	0.54
All four second premolars	24	1.08
Upper and lower second premolars	14	0.63
Upper lateral incisor and upper second premolar	28	1.26
Upper lateral incisor and upper and lower second premolar	30	1.35
More than 4 missing germs	31	1.39
Lower first incisor	23	1.04
Upper lateral incisor and lower first incisor	9	0.41
Lower first incisor and both lower premolars	5	0.22
Molars, other than wisdom teeth	15	0.68
Rare combinations	32	1.44
Total individuals with missing teeth	326	1.69

In 326 cases of the total patient number, one or more permanent tooth germs were found to be missing. Prevalence of hypodontia was 14.69%, with significant difference between male and female patients ($p<0.05$) (Table 3.2.1.1).

In 23 patients 6 or more congenitally missing permanent teeth were shown. These represented 7.05% of the total number of patients with hypodontia, and 1.04% of the total patient group.

For the different tooth types the sequence of hypodontia was as follows: upper lateral incisor > lower second premolar > upper second premolar > lower first incisor. The prevalence of hypodontia for the different tooth types is shown in Table 3.2.2.1. The cases with rare combinations were as follows: Upper central incisor: 9, all four upper incisors: 2, upper lateral incisor and first premolar: 2, all four lower incisors: 1, all four lateral incisors: 1. The study revealed 15 cases of missing molar germs, other than third molars. Among these, 4 patients presented symmetrical and isolated permanent molar aplasia.

3.2.3. Congenitally missing permanent canines – unpublished results

The findings revealed 13 cases of PCA. The prevalence was 0.29%. Permanent canine was found missing in the upper jaw in 9 cases, in the lower jaw in 4 cases, and in both upper and lower jaws in 3 cases. The prevalence of PCA was 0.27% in the maxilla, and 0.09% in the mandible. Statistical significance was noted between them by the χ^2 test with $p<0.01$. The male-to-female ratio was about 1:2. Three cases were isolated canine agenesis: two sisters, the older, aged 18 had all 4 permanent canines absent, the primary canines were persisting and showing root resorption grade 1 (Fig. 3.2.3.1.). This patient also had a root anomaly on tooth 22 and showed the presence of all wisdom tooth germs. The younger sister, aged 17 had both upper permanent canines missing, the primary canines were also present, root resorption grade 2 on the right side and grade 1 on the left (Fig.3.2.3.2.). The third case of isolated canine agenesis was a 15-year-old male patient missing both upper permanent canines. The primary canines were persisting, root resorption grade 0, the wisdom germs were also missing.

Findings revealed two cases, where all four permanent canines were missing: the first was described above, among the cases of isolated PCA; the second case was a 14-year-old female patient with her lower left second premolar germ also missing and talon cusp on the upper right lateral incisor (Fig. 3.2.3.3). All correspondent primary teeth were persisting, root resorption grade1.

Most cases were bilateral upper canine agenesis, a total of 6 such cases were recorded. Four of the patients with upper cuspid agenesis had the primary canines persisted, root resorption

grades are shown in Table 3.2.3.2. There was only one case of bilateral lower canine agenesis and one case with bilateral lower and unilateral upper missing permanent cuspid. Both were female patients. In the latter case of an 18-year-old patient, the x-rays confirmed the presence of persisting primary supernumerary lateral incisor in the lower arch.

Various complications of dental anomalies associated with PCA were found, as shown in Table 3.2.3.1.: 11 cases of persistent primary canines, 10 cases of other types of hypodontia of permanent germs, 1 case of primary supernumerary tooth, 1 case of supernumerary cusp, and nine cases of occlusal disturbances.

Table 3.2.3.1. *Dental anomalies and other complications accompanying permanent canine agenesis*

Clinical findings	Male	Female	Total
Persistent primary canine	5	6	11
Hypodontia of other permanent teeth, excluding the 3rd molars	4	6	10
Supernummerary primary teeth	-	1	1
Supernummerary cusps on permanent teeth	-	1	1
Malocclusions	4	5	9

Table 3.2.3.2. *Degree of root resorption of persistent temporary canines*

Permanent canine agenesis cases	Persistent temporary canines – Nr. of cases	Degree of root resorption		
		0	1	2
All permanent canines	2 of 2		2	
Bilateral upper permanent canines	4 of 6	1	1	2
Unilateral upper permanent canines	3 of 3	2	1	
Bilateral lower permanent canines	1 of 1	1		
Unilateral upper and bilateral lower permanent canines	1 of 1		1	

Legend: Degree of root resorption

- *0 - no or minimal*
- *1 - less than ½ of the root length*
- *2 - more than ½ of the root length.*

Fig. 3.2.3.1. 18 years old female patient with all four permanent canines missing.

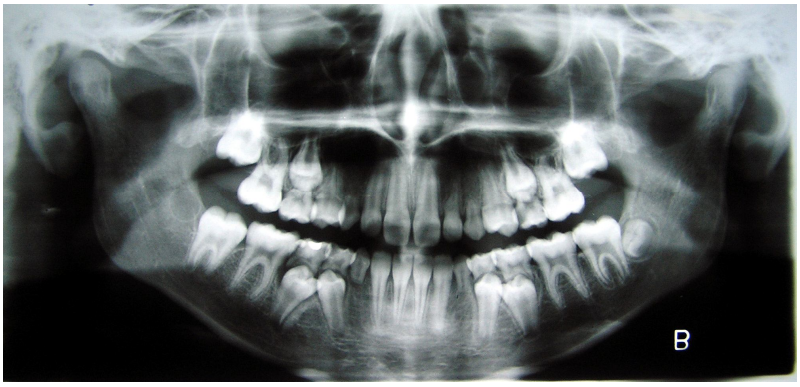


Fig.3.2.3.2. 17 years old female patient with bilateral upper permanent canine agenesis

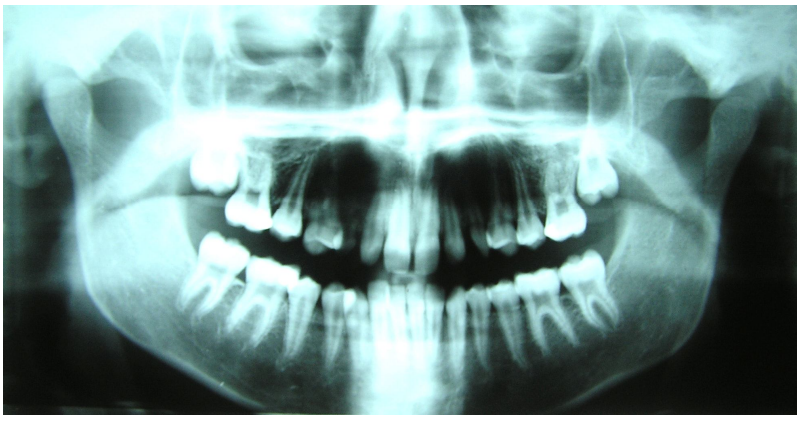
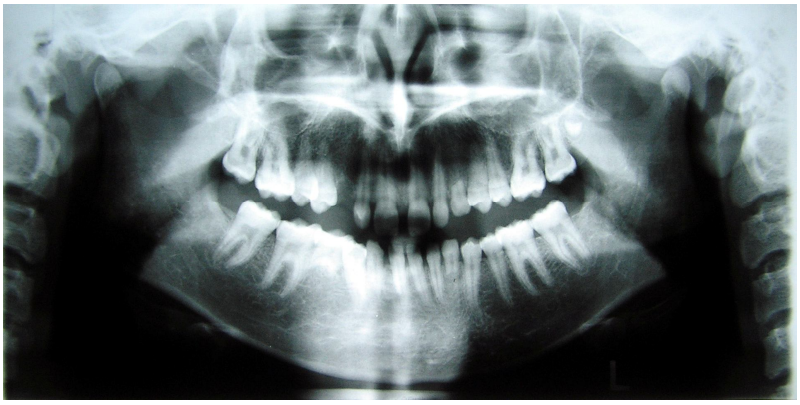


Fig. 3.2.3.3. 14 years old female patient with all four permanent canine and lower left second premolar missing.



3.3. Malpositions: Impacted upper permanent canines

Table 3.3.1. *Prevalence and distribution of impacted maxillary permanent canines.*

Impacted Canines	**Nr. of cases**	**%**
Total	101	5.43
Male*	46	6.08
Female*	55	4.99
Bilateral#	35	1.88
Unilateral#	66	3.55
Unilateral right**	35	1.88
Unilateral left**	31	1.66

* and ** $p>0.05$, # $p<0.001$,

The OPGs of the 1858 orthodontic patients (1102 female and 756 male) revealed a total of 101 cases of maxillary permanent canine impaction. Prevalence was 5.43%. The female: male ratio was approximately 1:0.8, with no significant difference between male and female occurrence ($p>0.05$). Bilateral maxillary canine impaction was shown in 35 cases, prevalence was 1.88%. There was significant difference between unilateral and bilateral distribution of impacted canines ($p<0.001$). In the group with unilateral localization, in 35 cases the impacted teeth were on the right side, in 31 cases they were located on the left. Prevalence values are shown in Table 3.3.1. There was no significant difference between the right and left localisation of the impacted upper permanent canines ($p>0.05$). 35 patients refused treatment (34.65%). The applied treatment methods for the rest of 66 patients (65.34%) with upper permanent canine impaction are shown in Table 3.3.2.

Table 3.3.2. *Applied treatment methods for impacted maxillary permanent canines.*

Treatment methods	Nr. of cases	%
Surgical exposure of the impacted canine and fixed orthodontic appliance	63	96.92
Extraction of the upper firs premolar and fixed orthodontic appliance	27	40.91
Surgical exposure of the impacted canine, extraction of the upper first premolar, extraction of the persisting primary canine, and fixed orthodontic appliance	8	12.12
Surgical exposure of the impacted canine, extraction of the upper first premolar, extraction of the persisting primary canine and first primary molar, followed by fixed orthodontic appliance	2	3.03
Spontaneous resolution after extraction of the upper firs premolar	2	3.03
Extraction of the impacted permanent canine on patients request	1	1.52

4. Discussion

4. 1. Accessory cusps

4.1.1. Carabelli cusps

The mostly detected dental characteristic, the Carabelli cusp, can be used to determine the degree of intercourse between populations with different racial characteristics (Gouse and Lee, 1971). Dahlberg's classification is the most commonly applied method for determining it's degree and expression (Kieser and Van der Merwe, 1984).

Dental characteristics can be divided into the so-called western-type (including Carabelli cusps) and to eastern-type (Kraus, 1951; Alvesalo *et al*., 1975). The frequency of a Carabelli cusp is high in Europeans, 70 to 90%, but low in oriental races (Alvesalo *et al*., 1975). The findings of the present study showed a prevalence of 65.34% in the contemporary group, and 34 per cent for the 11th century skulls, which are, in both cases, lower than the European average. In Malaysian children the frequency of a Carabelli cusp on the maxillary first molars was 54.2% (Rushman and Meon, 1991). In India 52.77% of maxillary first permanent molars displayed a Carabelli tubercle (Kanappan and Swaminathab 2001). Hassanali (1982) showed that the Carabelli's trait was present in 26-27% of Asian school children. Caucasoid populations differ from Mongoloids by having a high prevalence of Carabelli's trait (Hsu *et al*., 1997). As shown in different studies the intercourse between European and Mongoloid population leads to a reduction of total frequency of prevalence in the Europid population. (Kraus 1951; Palomino *et al*., 1977; Gianniou *et al*., 2000).

4.1.2. Talon cusps

The prevalence of talon cusps in the contemporary study group was 2.5%, compared with the high prevalence found on the skulls from the Árpád-era (40.8%). Chawla *et al.* (1983) found a prevalence of 7.7% in children from north India. The incidence of a talon cusp in the Chinese population is much higher than previously considered (Chen and Chen, 1986) and a prevalence of 52.2% has been reported in Malaysia (Rushman and Meon, 1991).

These morphological anomalies have great significance, both orally and anthropologically. The anatomy of the teeth can provide information on a population and as they are not often influenced by time, they can be studied on skeletons, and the development and changes of a population can be followed. The morphology and prevalence of Carabelli cusps can provide answers to many questions, such as division of a population into western or oriental type dentition, the mixture of races within a population, and the homogeneity of European and

oriental populations. A Carabelli cusp is more common in Europeans than Mongoloids and the talon cusp is less common in Caucasians than Mongoloids (Buenviaje and Rapp, 1984).

4.2. Numerical dental anomalies

4.2.1. Hyperdontia

The prevalence of supernumerary permanent teeth recorded in the present study (1.53%) is in accordance with the international data: 0.1 and 3.8% (Mitchell and Mitchell 1992, Stellzig *et al.* 1997, McKibben and Brearly 1971, Brook 1974). Many authors have reported sexual dimorphism: males are more affected than females, with a ratio of 2:1 (Egermark-Eriksson and Lind 1971, Rajab and Hamdan 2002). These data are in concordance with our findings, 1.84% among male and 1.31% among male patients.

The origin of supernumerary teeth is suggested to be due to a reversion to an atavistic trait; aberrant hyperactivity of the dental lamina; reactivation of the residues of the dental lamina; or a dichotomy of an initiated enamel organ which provides extra tooth buds (Gardiner, 1961; Berkovitz and Thopson, 1973). According to the atavism theory, the teeth, which disappeared during the course of evolution occasionally reappear in some descendent individuals. This would explain the higher prevalence of accessory teeth recorded in the anterior incisor and lateral premolar regions (97.5%) and their absence in the lateral molar region. 32.5% of the accessory teeth were identified as mesiodens.

4.2.2. Hypodontia

The accepted terminologies used for congenital tooth agenesis, listed in order of increasing severity are: aplasia; only one tooth is missing, hypodontia; up to 6 teeth missing, oligodontia; more than 6 teeth missing, and anodontia; complete absence of dentition (Silverman and Ackerman 1979, Burzynski and Escobar 1983). The prevalence of hypodontia in permanent dentition reveals great variations between populations. Recent reports concerning the Caucasian population presented the prevalence between 3.9% and 11.3% (Larmour *et al.* 2005). Relatively higher prevalence rate of 14.69% with no significant differences between male and female patients was recorded in our retrospective radiographic study. A similar Hungarian study in Debrecen showed prevalence of 7.68% (Szepesi *et al.* 2006). These variations in the statistical data are due to multiple causes, such as different sample-taking procedures. The sequence of hypodontia for the different tooth types was as follows: upper second incisor – lower second premolar – upper second premolar – lower first inscisor, but no case of missing permanent canines was found. These data correlate with Butler's Field Theory related to mammalian teeth, which states that the most mesial situated tooth is the

most stable in each morphological class, and so the canine being the sole representative element in its developmental field, should be the most stable and rarely missing tooth (Butler 1939).This theory has been adapted to human dentition by Dahlberg (1945). He stated that in each developmental field in a tooth-group there is a genetically stable "key tooth", while at the end of the "field" the teeth show less stability (Dahlberg 1945; 1949). According to this theory Bailit (1975) explained the distribution of hypodontia in permanent dentition by classifying the teeth into groups of stable and unstable teeth. Thus the upper canines are considered stable, along with the upper central incisors, the first premolars, and the first molars (Cabov *et al.* 2006).

4.2.3. Congenitally missing permanent canines

Congenital canine agenesis is considered a rare condition (Lombardo *et al.* 2007), and it has been described mainly in oriental populations (Davis 1987, Lum and Lim 1976, Cho and Lee 2004, Cho *et al.* 2004). The statistical data on cuspid agenesis differ greatly in the literature. The differences to the prevalence values are due to various causes, such as disagreement in sample analysing, as these studies are most frequently carried out on selected patient groups. Comparative prevalence data of PCA can be seen in Table 4.2.1.: prevalence ranges from 0.01 to 2.10%. Our findings revealed a prevalence of 0.29%, similar to the data of Fukuta *et al.* (2004), who reported a prevalence of 0.18%, Hokari *et al.* (2000), who showed a prevalence of 0.23% in Japanese population. In European studies Bergström (1977) recorded similar prevalence results, 0.23%, on Swedish school children.

Muller *et al.* (1970) found five cases of missing maxillary canines among 13 459 white American schoolchildren, a prevalence of 0.037% and two cases out of 1481 Afro-American children (prevalence 0.14%) in the same study. Fekonja (2005) recorded only one case of upper PCA amongst 212 orthodontic patients in Slovenia, prevalence 2.1%. The prevalence of missing maxillary canines recorded in the present study was 0.27%. This is similar to the data presented in Table 4.2.1 from studies of Japanese (Hokari *et al.* 2000, Fukuta *et al.* 2004), Chinese (Davis 1987), and Swedish (Bergström 1977) children. All of the series presented in Table 4.2.1 recorded higher prevalence of PCA in the maxilla than in the mandible, only Altug-Atac and Erdem reported a prevalence of 0.07% in the lower jaw in Turkish patients and no case of canine hypodontia in the upper jaw. The results of the present study are in accordance with the data in the literature: the difference between the prevalence in the maxilla (0.27%) and in the mandible (0.09%) was significant ($p<0.05$).

The congenital absence of permanent canines was reported to be higher in female patients (Fukuta *et al.* 2004), which was in accordance with the present findings of a male-to-female ratio of 1:2.

In the present study, bilateral upper canine agenesis was the most frequent distribution form, in 6 cases, with prevalence of 0.13%. Cho *et al.* (2004) described congenitally missing upper permanent canines in 32 Chinese children. Nine out of 32 cases were bilateral. Fukuta *et al.* (2004) found 16 cases of multiple canine absences in the upper jaw. These data correlate with our findings: 5 of the 6 cases of bilateral maxillary canine agenesis were detected

The occurrence of bilateral mandibular PCA is even rarer. Cho and Lee (2004) presented six cases of hypodontia involving only lower permanent canine, all cases were of Chinese ethnicity. Two cases were bilateral. Fukuta *et al.* (2004) described among Japanese children 6 cases of bilateral permanent canine absence. Our present findings revealed a single case of bilateral lower canine agenesis, with a prevalence of 0.02%.

In the literature single canine absence is more predominant than multiple absences and it occurs mostly combined with other types of hypodontia. Fukuta *et al.* (2004) reported a total of 37 cases of single canine absence, 26 in the upper jaw, and 11 in the lower jaw. There was a predominance of absence at the left of the maxilla ($p<0.01$) and at the right mandible ($p<0.05$). Altug-Atac and Erdem (2007) found 2 cases of unilateral mandibular canine agenesis; prevalence was 0.07%. Cho and Lee (2004) reported 4 cases of unilateral lower PCA in 6 Chinese children, with no significant difference between the right and the left sides. In our series only 3 cases of unilateral upper PCA were recorded. No unilateral lower cuspid agenesis case was found. The prevalence of the upper unilateral findings was 0.06%. High incidence score was reported by Fekonja (2005) in 212 Slovenian orthodontic patients, a prevalence of 2.1%, similarly to the results of Cabov *et al.* (2006), who found 1 case of upper PCA - prevalence 3.7% - in a sample group of 27 archaeological findings of jaw and teeth remains dating from the 9th to the 11th century in an early Croatian cemetery. These large differences between our findings and the results of Fekonja (2005) and Cabov *et al.* (2006) can be explained by their relative small sample number.

Fukuta *et al.* (2004) recorded 10 cases with all four permanent canines missing, 4 male patients and 6 female patients. None of the cases were isolated canine agenesis, and the primary cuspids were persisting. Huggare (1984) described one isolated case of all cuspid agenesis. Bótyik *et al.* (1977) presented one case of a Hungarian patient with isolated complete aplasia of the permanent canines. Our findings revealed 2 cases of complete canine agenesis in permanent dentition; prevalence was 0.02%. The first case of an 18-year-old girl

had a family character; her sister presenting a bilateral upper PCA. This patient had also a root anomaly on tooth 22 and showed the presence of all wisdom tooth germs. The second case was a 14-year-old female patient with her lower left second premolar germ also missing. In her case no other family member was affected by any form of hypodontia. In both cases the primary cuspids were persisting, with root resorption grade 1.

Fukuta *et al.* (2004) found 8 cases of 3 canine agenesis, 3 male, and 5 female patients. The canines missing were in all cases teeth 13, 23 and 33. Our study recorded only one rare case of a female patient with 3 missing permanent canines: 23, 33 and 43, prevalence was 0.02%.

There seems to be a correlation between fusion and agenesis in primary dentition and congenital absence of the permanent successor (Fukuta *et al.,* 2004). In the present study 10 cases were combined with other types of missing permanent germs.

Ramaraj and Mirza (1995) described one case of bilateral congenitally missing madibular canines associated with a supplementary lower incisor. Another case with a single missing canine and concomitant multiple supernumerary teeth was presented by Sharma (2001). The radiological findings of the present study revealed a rare case of a female patient described above with bilateral lower and unilateral upper missing permanent cuspids and concomitant persisting primary supernumerary lateral incisor in the lower arch. The upper primary canine was persisting with root resorption grade 1. The mother also presented hypodontia. Another case of a male patient was found with upper left canine agenesis, combined with persistent primary canine – root resorption grade 1 – lower left second premolar agenesis and supernumerary talon cusp on the left upper lateral incisor. Fukuta *et al.,* (2004) described a similar case of a missing permanent canine associated with a talon cusp. This type of supernumerary cusp has a tendency to be complicated with other dental abnormalities (Mader, 1981). Malocclusions were found in 9 cases (69%). Our value is much higher than the 23 cases with orthodontic anomaly (10%) reported by Fekonja (2005) and the results of Fukuta *et al.,* (2004) who found 6 cases of occlusal disturbances (9.2%). The discrepancies in these results can be attributed to the variable sampling criteria: our study was carried out on a selected orthodontic and paedodontic patient group.

Hypodontia in permanent dentition is usually accompanied by retention of primary teeth. According to Haselden *et al.* (2001) the persisting deciduous canines are more likely to show minimal root resorption. In the present study persistent primary canines were present in 11 cases, the most frequently recorded root resorption degree was 0 in 4 cases, one in 5 cases, and only two cases showed advanced primary root resorption (Table 3.5.2). Retaining the persistent primary canines is of considerable value in treatment planning. The persistent

deciduous teeth with minimal root resorption can preserve the dental arch integrity, providing good potential for later prostethic rehabilitation. Another therapeutic choice is the extraction of the primary canines, orthodontic space closure followed by second incisor and first premolar coronoplasty (Lombardo *et al.* 2007).

Table 4.2.1. *Comparison of prevalence data for permanent canine agenesis in the literature*

Authors	Total patient nr.	Maxilla		Mandible		Total	
		Nr. of cases	%	Nr. of cases	%	Nr. of cases	%
Dolder (1937)	10000	6	0.06	0	0	6	0.06
Rose (1966)	6000	6	0.10	1	0.02	7	0.12
Bergström (1977)	2589	4	0.15	2	0.08	6	0.23
Davis (1987)	1093	5	0.45	0	0	5	0.45
Hokari *et al.* (2000)	1524	6	0.20	1	0.07	4	0.26
Fukuta *et al.* (2004)	35927	48	0.13	23	0.06	65	0.18
Fekonja (2005)	212	1	2.10	0	0	1	2.10
Altug-Atac and Erdem (2007)	3043	0	0	2	0.07	2	0.07
Present study (2008)	4417	12	0.27	7	0.09	13	0.29

4.3. Malocclusions: Impacted upper permanent canines

Excluding the retention of the third molars, the sequence of permanent tooth impaction is as follows: upper permanent canines < lower second incisors < upper first incisors < upper premolars. The prevalence of impacted upper permanent canine described in the literature varies: less than 0.8% (Shah *et al* 1978), 0.9 % (Bass 1967), 2.8% (Grover and Lorton 1985) and 3.3% (Moss 1972). The data of the present study showed a higher prevalence rate: 5.44%. The discrepancy between the data in the literature and the registered data may be due to the selected orthodontic patient group studied. For individual orthodontic practice a much higher incidence (23.5%) is speculated (Ferguson 1990).

The occurrence is reported to be more than twice higher in girls (1.2%), than in boys (0.5%) (Dachi and Howell 1961). Sinkovits and Polczer (1964) registered in 5134 Hungarian patients aged 15 to 19 years a prevalence of 1.76% for female and 1.52% for male patients. Even higher discrepancies were shown for young adults (Adler-Hradeczky and Polczer 1960). In our study for the 101 cases with maxillary impaction the male:female ratio was 0.8:1, with no significant difference between male and female occurrence ($p>0.05$). But considering the total patient number the occurrence of the anomaly was 4.99% for girl patients, and a higher rate, 6.08% was registered for boys. Similar data were found in a study of 2000 schoolchildren: 5.6% for boys, and 4.1% for girls (Schopf 1991).

It is not unusual for maxillary canine impaction to occur bilaterally, although unilateral ectopic eruptions are more frequent (Shapira and Kuftinec 1998). This is in accordance with the data registered in the present work: there was a significant difference between unilateral (3.55%) and bilateral distribution (1.88%) of impacted canines ($p<0.001$). In the group with unilateral localization, in 35 cases the impacted teeth were on the right side (1.92%), in 31 cases (1.70%) they were located on the left (Table 3.3.1.) Similar to the data in the literature, there was no significant difference between the right and left localisation of the impacted upper permanent canines ($p>0.05$) (Moss 1972).

The impacted permanent canine often requires a complex multidisciplinary treatment, involving oral surgical, restorative, periodontic, as well as orthodontic components (Bishara 1994. In our study 35 patients refused treatment (34.65%). Among the reasons were frequent the refusal of permanent tooth extraction, minor aesthetical problems, the absence of other symptoms, like pain and discomfort during mastication. Other objection was also the time-consuming and expensive orthodontic treatment.

The following treatment alternatives are considered in cases of upper permanent canine impaction: interceptive treatment with extraction of the persisting deciduous canine; surgical exposure and the application of fixed orthodontic appliance to align the canine, autotransplantation of the canine, extraction and movement of the first premolar in its position, prosthetic replacement or implant application, if the patient refuses treatment, monitoring the impacted tooth for any pathological changes (Bishara 1994, McSherry 1998)

In the present study the applied treatment methods for the rest of 66 patients (65.34%) with upper permanent canine impaction are shown in Table 3.3.2. The female-male rate was 1:0.6, similar to the data in the literature, explained by higher aesthetical expectations for girl patients (Baergen and Baergen 1997). Surgical exposure of the impacted canine and fixed orthodontic appliance application was necessary in 96.92% of the treatment cases. In 40.91% of the cases extraction of the upper first premolar preceded the orthodontic treatment. Spontaneous resolution after extraction of the upper firs premolar was registered in 3.03%. These data show the importance of early detection and a possible prevention of permanent canine impaction by extraction of the persisting primary canine to decrease patient's need for oral surgery and simplify orthodontic treatment (Warford *et al* 2003). Extraction of the impacted permanent canine on patients request was necessary in one case. Surgical removal is indicated generally if there is a poor patient co-operation or poor position for alignment (oblique or horizontal position) with a concomitant good lateral incisor/first premolar contact and the possibility of internal and/or external rooth resorption of teeth adjacent to the

impacted canine (McSherry 1998). The dental practitioner should be aware of dental anomalies that occur with impacted maxillary canines. Early intervention can spare the patient time, expense, more complex treatment and injury to otherwise healthy teeth (Richardson and Russel 2000). These patients undergo a comprehensive assessment for canine localization and alignment prognosis. This can be influenced by patient age, skeletal variations and arch condition (crowding) (McSherry 1998). Because of patient age among patient information a meticulous parent counselling and informed consent is needed to avoid later medico legal problems (Machen 1989).

5. Clinical reports

5.1. Early prosthetic treatment of patients with ectodermal dysplasia

5.1.1. First Patient

A 3-year and 11-month-old male patient presented to the Department for Paedodontics and Orthodontics, Semmelweis University Budapest. for speech and masticatory difficulties due to several missing primary teeth. The boy was the second male affected in three generations. The information collected during the initial interview revealed affected maternal family members. The mother also presented with anodontia of the upper central and lateral incisors. The grandmother's sister had complete anodontia and hypohidrosis, and her son also presented severe hypodontia with only 6 permanent teeth present.

Extraoral examination: The child exhibited the classical features of hypohydrotic ectodermal dysplasia (HED) including diffusely sparse hair, eyelashes and eyebrows, severe hypohidrosis, and subsequent problems with thermoregulations and dry skin. Hypotonicity of both the peri-oral and masticatory muscles was detected. The facial profile showed a sunken nasal bridge, the so-called "saddle-nose", with prominent forehead and everted lips.

Cephalometric radiograph analysis revealed a reduced vertical dimension of occlusion of the lower third of the face. The facial height index of 105% as compared with the ideal score of 80% (Hasund and Ulstein, 1970) included an extremely decreased vertical dimension of occlusion (Fig. 5.1.1.1.).

Intraoral examination: The patient presented macroglossia, a slightly dry and sticky oral mucosa, and severe hypodontia. Only the maxillary second primary molar was present in the oral cavity (Fig. 5.1.1.2.).

The clinical findings were confirmed by radiographic examination (Fig. 5.1.1.3.)

Treatment planning: Considering the clinical situation and patient age, upper removable partial dentures and lower complete dentures were determined to be the treatment of choice.

Treatment: Preliminary impressions - with irreversible hydrocolloid - and definitive impressions were made. After maxillo-mandibular records, the casts were mounted in articulator. The artificial teeth were arranged in wax for trial evaluation. Prosthetic teeth shaped as primary teeth were chosen to achieve an age-appropriate appearance for the child. The position of the artificial teeth and the occlusion were intraorally evaluated, and the necessary corrections were made before processing the dentures (Fig. 5.1.1.4.).

Facial-height index measurements made after inserting the prostheses showed approximately normal values: 79% (Fig. 5.1.1.5.) The patient was monitored every 3 month.

The accommodation to both upper and lower dentures occurred relatively rapidly, with considerable improvements of speech and masticatory function for our young patient. The dentures had to be remade 8 month later due to the growth of the jaws (Fig. 5.1.1.6.)

5.1.2. Second patient

A 3-year, 2-month-old male patient presented to the Department for Paedodontics and Orthodontics, Semmelweis University Budapest. for examination, evaluation, and treatment.

The patient presented thin, diffusely sparse blond hair, eyelashes, and eyebrows (Fig. 5.1.2.1.). Sever hypohidrosis and fingernail defects were also detected (Fig. 5.1.2.2.). The body skin appeared to be extremely dry, pale, and hairless. Generally, his face had a more "aged" appearance (Ramos *et al.* 1995). In profile he showed prominent lips, a depressed nasal bridge, and a vertically reduced occlusal dimension (Fig. 5.1.2.3.).

Intraoral examination showed two upper second primary molars and a complete absence of the lower teeth were detected (Fig. 5.1.2.4.). On the panoramic radiograph both maxillary second primary molars, the right upper canine, and all 4 first permanent molars were evident (Fig. 5.1.2.5.).

Treatment planning and treatment: Early removable prosthetic treatment, similar to the first HED patient was indicated. Upper removable and lower complete dentures, fabricated as previously described, were inserted. The one notable exception in the procedures of denture fabrication used during the treatment of the first patient was the lingualized occlusion used to reduce lateral forces and to create intercuspal contact area with freedom of movement (Fig. 5.1.2.6.) (Bonilla *et al.*1997, Lekholm 1993, Pigno *et al.*1996). In order to prevent lateral interference, the lingual cusps of the maxillary posterior teeth contacted the fossae of the mandibular teeth. The dentures contributed to the development of harmonious facial proportions (Fig. 5.1.2.7.). The patient was monitored and the parents reported only minor problems during the adaptation period. Significant speech and aesthetic improvements, and a general well-being, including a better social adaptation of the child were achieved.

5.1.3. Discussion

The EDs represent a large and complex nosological group of congenital diseases, first described by Thurman in 1848 (Priolo and Lagana 2001). EDs are relatively rare and they are characterized by abnormal development of embryonic ectoderm derivates (Johnson et al. 2002). The triad of nail dystrophy (onchodysplasia), alopecia or hypotrichosis (scanty, fine light hair on the scalp and eyebrows) and palmoplantar hyperkeratosis is usually accompanied by lack of sweat glands (hypohidrosis) and partial or complete absence of primary and/or permanent dentition (Taylor *et al.* 1998, Bonilla *et al.* 1997). There are two categories of ED, the hidrotic and the hypohidrotic forms. Dentition and hair are affected similarly in both forms, but hereditary patterns nail and sweat gland manifestations tend to differ (Bonilla *et al.* 1997).

Hypohidrotic ectodermal dysplasia (HED) with an X-linked recessive inheritance is the most frequently reported ED syndrome and it affects severely and more frequently males, while female heterozygotes present minor defects. The incidence of HED, known also as Clouston or Christ-Siemens-Touraine syndrome, is about 1/100,000 (Clouston 1939, Buyse 1990, Saksena and Bixler 1990,). Hypodontia of primary and permanent dentition is the second most frequently occurring oral symptom, associated with hypoplasia of the alveolar bone structures with poorly formed ridges (Jaskoll *et al.* 2003, Guckes *et al.* 2002). The number of missing teeth varies, with higher incidence in the lower jaw. In the primary dentition maxillary second molars, canines, central incisors and mandibular canines are the most commonly present. Teeth that do develop are often conical in shape, complicating their utilization as partial denture abutments but sometimes offering the possibility to use them for complete overdentures (Abadi *et al.* 1982, Levin 1988).Severe maxillary hypodontia in permanent dentition has proved to be related to craniofacial dysmorphology affecting cranial base and mandibular length, in the male ED population (Johnson *et al.* 2002).

Oral rehabilitation of the HED patient is recommended to improve both sagittal and vertical skeletal relationship during craniofacial growth and development, as well as to provide substantial benefits to aesthetics, speech and masticatory efficiency (Bonilla *et al.* 1997).

Prosthetic treatment using partial or complete dentures and application of oral implants are the main rehabilitation alternatives for the clinical management of young patients with severe hypodontia. Oligodontia or anodontia totalis associated with ED is often characterized by underdeveloped alveolar bone structures with missing or reduced alveolar ridges. This results in less volume of bone for support of conventional prosthetic dentures and it can also affect

the bone volume available for the placement of dental implants (Guckes *et al.* 2002). In developing the optimal surgical and prosthetic approach, the patient1s age, dental and skeletal maturity and the bone volume that is available at the time of intervention must be considered (Imirzalioglu *et al.* 2002). Placement of endosteal implants is not suggested during the time of maxillary growth, determined as being up to 15 years of age (Lekholm 1993). Early prosthetic treatment is recommended generally from the age of 5 years. According to our opinion, dentures can be applied earlier, at the age 3 to 4 years for cooperative children.

Applied early, dentures can lead to significant improvement of appearance, speech and masticatory function (Ramos *et al.* 1995). The positive changes increased the self-confidence of the children presented above, as described by the psychologists and the speech definitely improved, according to speech therapist.

The restoration of the natural and pleasing appearance is important for the normal psychological development of HED children and their future social integration. Although dentures are poor alternatives to a healthy dentition, they create conditions for the maintenance of a normal, satisfactory daily diet for the child. This is very important, considering that establishment of life-long dietary patterns happens during childhood (Bektor *et al.* 2001). Non-functional speech problems are also proven to improve after dentures were applied to edentulous children (Mitchell and Grant 1976, Riekman and el Badrawy 1985, Ramos *et al.* 1995).

Problems with early complete dentures are related to growth and development and, also, to the cooperation of the child. In each situation, parents should be aware of the possibility that the young patient may refuse the treatment procedure and may not wear the dentures (Ramos *et al.* 1995). Removable partial or complete dentures require regular adjustments and shoul be replaced when a decreased vertical dimension of occlusion and an abnormal mandibular posture are detected due to growth. Without dentures, the antero-rotation of mandible causes an upward and forward displacement of the chin with reduction of the height in the lower third of the face, and tendency to Class III malocclusion. The presence of dentures allows a backward-downward rotation of the mandible, with consequent normal positioning of the chin in the space (Franchi *et al*. 1998). Saisfactory retention and stability of the prosthses is also difficult to obtain. In HED patients, dryness of oral mucosa and the underdeveloped maxillary tuberosities and alveolar ridges are problematic factors for resistance and stability of dentures (Shaw 1990). When planning dentures in this cases, care should been taken to obtain a wide distribution of occlusal load fully extending the denture base. The remaining anterior teeth, due to their atypical conical shape, may not be suitable for denture stabilization. However,

they may be used as abutments for complete overdenture (Dyson 1988, Abadi *et al.* 1982, O'Dwer *et al.* 1984). Also special attention must be paid to the impression technique, for complete dentures it should not be limited to the denture base area, but should also include the entire vestibular sulcus reflection for a retentive base construction with border seal (Dyson 1988). For optimal aesthetic results, denture teeth should be age-appropriate (Ramos *et al.* 1995). For partial dentures, the occlusion should be in harmony with the patient's occlusion; generally an occlusal scheme utilizing linear occlusal contact is recommended to preserve the existing teeth and to create freedom of movement (Bonilla *et al.* 1997). Some authors suggest the insertion of one denture at a time to facilitate accommodation (Pigno *et al.* 1996). In the cases presented, the social condition of the families made it impossible to first make the dentures for the arch with the better prognosis, but accommodation problems were negligible.

Fig. 5.1.1.1. The facial height index 105%, compared to the ideal score of 80% according to Hasund measurements, indicated extreme vertical depression.

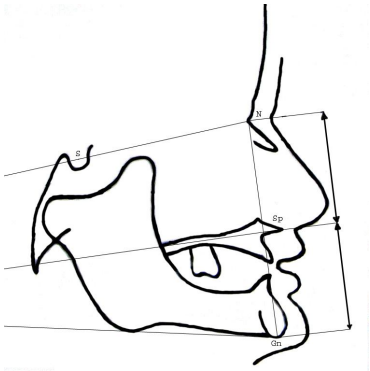


Fig. 5.1.1.5. Facial height index measurements after applying dentures show approximately normal value (79%).

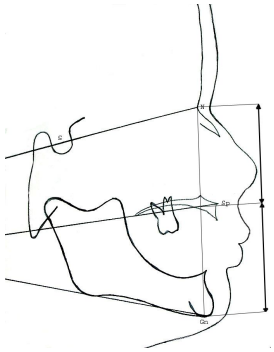


Fig. 5.1.1.2. Intraoral examination revealed severe hypodontia, only teeth 55 and 65 were present.

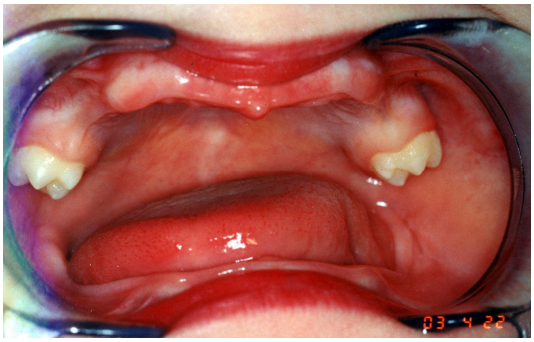


Fig. 5.1.1.3. Panoramic X-ray proves the clinical findings.

Fig. 5.1.1.6. Eight months later, the dentures had to be changed due to the growth of the upper and lower jaws.

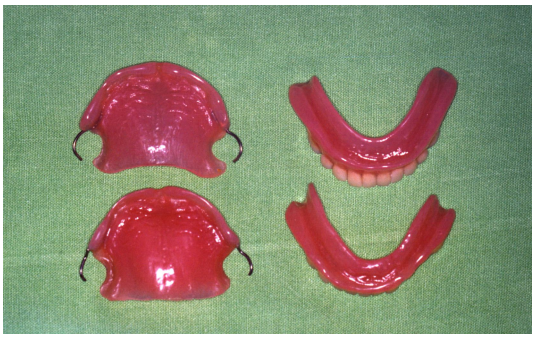


Fig. 5.1.1.4. Dentures in situ.

Fig. 5.1.2.1. Patient with thin diffusely sparse blond hair, eyelashes and eyebrows.

Fig. 5.1.2.2. Fingernail defects.

Fig. 5.1.2.4. Clinical oral examination revealed two upper second primary molars in the maxilla and no teeth in the mandible.

Fig. 5.1.2.5. On panoramic X-ray, the right upper canine and the four permanent molars could be seen besides the two upper second primary molars.

Fig. 5.1.2.3. Patient profile with prominent lips, depressed nasal bridge and reduced vertical dimension of the lower face.

Fig. 5.1.2.7. Lateral facial photo with dentures shows a harmonious proportion of the face.

5.2. Tuberculate and Odontoma Type Supernumerary Teeth:

5.2.1. Third patient

An 8-year-old female patient presented at the Department for Paedodontics and Orthodontics, Semmelweis University Budapest. with severe aesthetic problems. The patient was healthy, with no family history of developmental dental anomalies.

Intraoral examination: upper right primary canine, first, and second primary molars, left permanent canine, and primary second molar could be detected in the maxillary dental arch. In the mandible, both left and right first and second primary molars were present. The maxillary second primary and first permanent molars had Carabelli cusps. Two permanent central incisors showed barrel-shaped form, and the permanent upper lateral incisor showed talon cusp Type 2 according to Hattab *et al*. (1994) (Fig. 5.2.1). The lower permanent incisors were all of normal size, shape and colour. They were fully erupted in reasonable alignment.

Radiological examination: OPG was taken and they showed the two upper central incisors presumably with dente invaginati and two supernumerary teeth situated bilateral in anterior region. The supernumerary teeth appeared to be tuberculate type (Fig 5.2.2.). Periapical radiographs confirmed that the erupted upper central incisors presented invaginations, but did not give any further information about type and shape of the impacted maxillary supernumerary teeth (Fig. 5.2.3). At the time of the first clinical and radiological examination of the patient, there was no evidence of supernumerary tooth in the mandible. A year later, the

new OPG showed the maxillary right first premolar located between the roots of the permanent lateral and central incisors. On the left side the two upper premolars were located on top of each other. The formation of a supernumerary tooth located in the lower left premolar area was also seen on the OPG (Fig. 5.2.4).

Treatment planning: The orthodontic diagnosis was Angle class III with severe anterior open bite. A combination of surgical and orthodontic treatment on conventional lines was suggested.

Surgical and Orthodontic Treatment Technique: Because the radiographic examination did not provide enough information about size and shape of the impacted maxillary supernumerary teeth, surgical exposure was performed. The two upper supernumerary teeth were bigger in size but normal in shape and colour. Therefore the two erupted barrel-shaped central incisors were extracted (Fig. 5.2.5). Two metal brackets were placed on the surgically exposed supernumerary teeth. After soft tissue healing, elastic forces were applied to the supernumerary incisors with the help of a removable appliance to align them into the upper arch (Fig. 5.2.6). When secondary dentition was completed, the maxillary right first premolar was surgically removed. The upper left first premolar and both lower first bicuspids were extracted due to severe crowding. The odontoma type supernumerary tooth located at the lower left premolar area was also surgically removed. Fixed, multibracket orthodontic appliance was applied to align the teeth (Fig. 5.2.7). One year later, after the active part of the orthodontic treatment was finished; the fixed appliance was removed (Fig. 5.2.8), and retention plates were applied to the patient.

5.2.2. Discussion

In the case of suspected presence of supernumerary teeth a panoramic radiograph is indicated, although the OPG has a tendency of distortion, mainly in the anterior area. According to McVaney and Kalkwarf's (1976) suggestion, a periapical radiograph was also taken in order to confirm the diagnosis and to decide which teeth should be extracted. In the presented situation although the two types of radiographs were made, they did not give enough information to decide which teeth should be removed, surgical exposure was necessary.

In general supernumerary teeth are detected through clinical and radiographic examination. Treatment depends on the type and position of the supernumerary tooth and on its effect on the adjacent teeth. Most erupted supernumerary teeth are abnormal in size and shape, so they are extracted on aesthetic grounds (Camillieri 1976). In this case the upper barrel-shaped supernumerary teeth hindered the two upper incisors in eruption and they were unacceptable

aesthetically, so immediate removal of the supernumerary teeth was indicated. According to Munns (1981), the earlier the offending supernumerary tooth is removed, the better the prognosis. The lower supernumerary premolar had to be removed very cautiously to avoid surgical complications due to the close proximity of the inferior alveolar and mental nerves in the lower region.

Foster and Taylor (1969) stated that tuberculate supernumerary teeth rarely erupt and are frequently associated with delayed eruption of the incisors or of the permanent adjacent teeth. In the present case, the situation was similar, although the two supernumerary teeth of tuberculate type erupted. Also, there was no family history, which is in contrast with many published cases of supernumerary teeth that mentioned recurrence within the same family (Mason et al. 1996). Environmental factors can play an important role in the development of hyperdontia.

Patients should be regularly monitored considering the increased risk of further supernumerary teeth developing, like in the mandibular premolar region in the presented case (Moore *et al.* 2002).

Fig. 5.2.1. Two barrel-shaped upper central incisors and upper left lateral incisor with talon cusp.

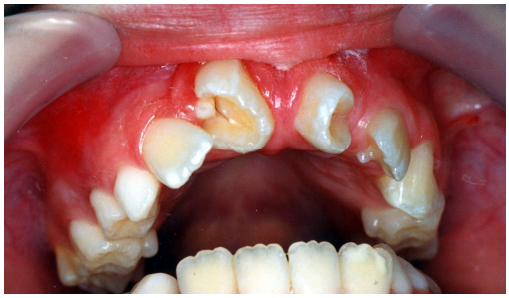
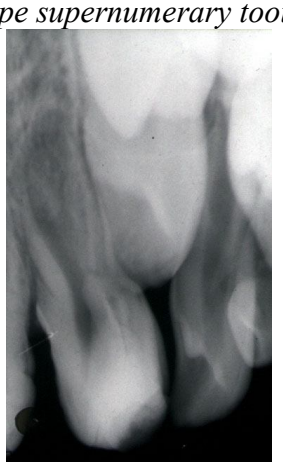


Fig. 5.2.2. Orthopantomogram revealing two maxillary supernumerary teeth in the anterior region.

Fig. 5.2.3. A. Invaginated maxillary right central incisor and a tuberculate type supernumerary tooth.



B. Invaginated left upper central incisor and a tuberculate type supernumerary tooth.

Fig. 5.2.4. Orthopantomogram showing the lower supernumerary tooth in the left premolar area.

Fig. 5.2.5. Surgical exposure of the normal shaped incisors.

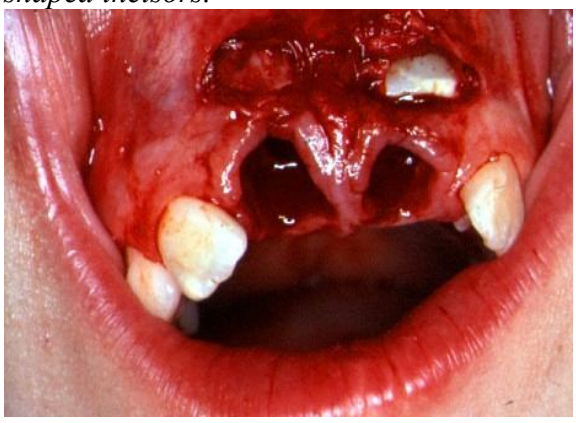


Fig. 5.2.6. Incisors are aligned with a combination of fixed and removable appliance.

Fig. 5.2.7. One year after orthodontic treatment with fixed appliance.

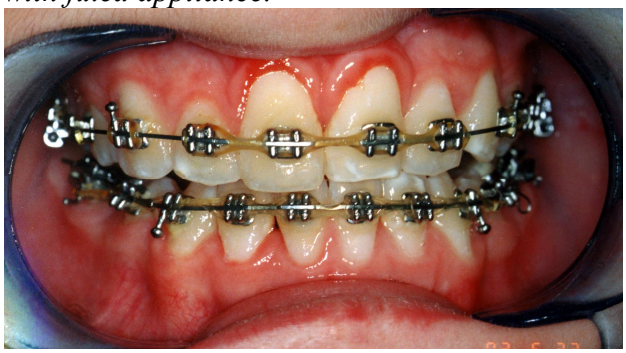


Fig. 5.2.8. The occlusion at the end of treatment.

5.3. Talon cusp, upper permanent canine ectopia

5.3.1. Fourth patient

A 10 year old male patient presented to our clinic for diagnosis and treatment. Clinical findings showed Angle class I. occlusion. The upper permanent second incisor presented a Type 1. palatal talon cusp (Hattab et al. 1996). In the lower arch the left second primary molar was persisting. Radiological analysis revealed lower left second premolar aplasia and complete absence of permanent third molar germs (Fig. 5.3.1. and 5.3.2.). Family history revealed a16-year-old brother with right upper permanent second incisor and left upper permanent canine aplasia.

Treatment plan and treatment:

- Step-wise grinding (1 mm/month) of the talon cusp to prevent occlusal interference in the anterior region (Fig. 5.3.3. and 5.3.4.).
- Multibond fixed orthodontic appliance in the maxilla after eruption of the ectopic upper canines (Fig. 5.3.5. and 5.3.6.)

Fig. 5.3.1. OPG of the patient before treatment

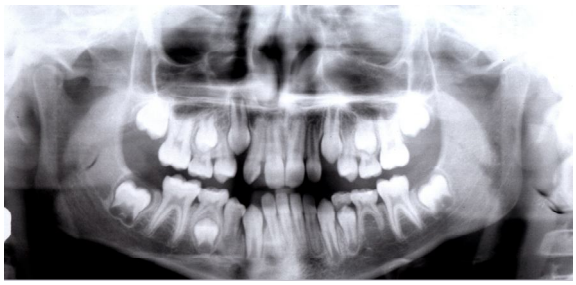


Fig. 5.3.2. Eruption of the upper right second incisor with palatal talon cusp

Fig. 5.3.3. Upper right second incisor before grinding of the talon cusp

Fig. 5.3.4. Upper right second incisor after grinding of the talon cusp

Fig. 5.3.5. Bilateral upper permanent canine ectopia before orthodontic treatment

Fig. 5.3.6. Multibond upper fixed appliance

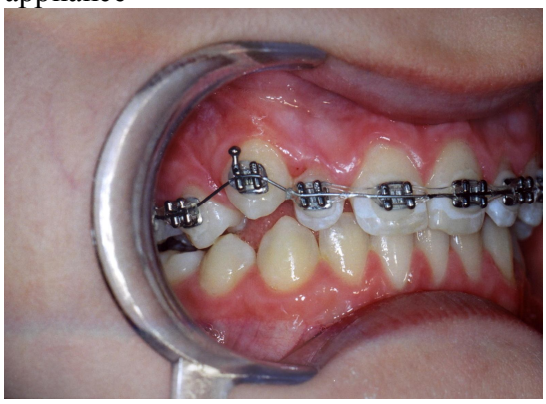
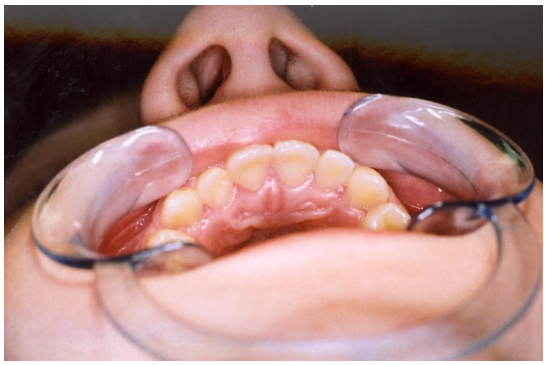


Fig. 5.3.7. After treatment view of the patient

Fig. 5.3.8. Occlusal view of the upper arch after orthodontic treatment



5.3.2. Discussion

The prevalence of talon cusp is in the Hungarian population 2.5% (Mavrodisz *et al.* 2003). It is more frequent in male patients (Mavrodisz *et al.* 2003, Takashi *et al.* 1996). In the permanent dentition it occurs isolated or combined with other developmental tooth anomalies, like Carabelli cusp, hyperdontia (Hattab *et al.* 1996, Mavrodisz *et al*. 2003). In the presented case it was associated with permanent canine malposition and aplasia of the lower second premolar. One of the most frequent disturbances caused by the cusp morphology is the occlusal interference during intercuspidation, and/or reversible acute apical periodontitis of the opposing tooth (Segura-Egea *et al.* 2003, Bolan *et al.* 2006). This can be prevented by the step-wise grinding grinding of the palatal cusp, 1 mm/month to allow secondary dentin formation. Because of the slow eruption of the lateral incisor the application of $Ca(OH)_2$ on the exposed surface was not necessary (Andlaw and Rock 1996). After complete eruption of the ectopic upper canines, fixed orthodontic appliance was applied for 8 month, followed by a 1.5 year conventional retention phase (Fig. 5.3.7. and 5.3.8.).

5.4. Permanent canine agenesis (PCA)

5.4.1. Fifth Patient

A 16-year-old patient presented for treatment with absence of right upper permanent second incisor. Clinical findings revealed diasthema medianum, left upper persisting primary canine and Angle class I. Radiological examination confirmed the right upper permanent second incisor aplasia and the left upper PCA (Fig. 5.4.1). Both lower third molar germs were present. The patient was the brother of the above described patient with bilateral upper permanent canine ectopia.

Treatment plan and orthodontic treatment:

- Multibond upper fixed orthodontic appliance (Fig. 5.4.2. and 5.4.3.)
- Reconstruction of the crown of the persisting primary canine (Fig. 5.4.4.)
- Prosthetic treatment for replacement of the upper right permanent lateral incisor

The patient refused the application of the lower fixed appliance necessary to align the lower teeth and to achieve an equilibrate occlusion.

Fig. 5.4.1. OPG of the patient during orthodontic treatment

Fig. 5.4.2. Multibond appliance in situ

Fig. 5.4.3. Space gaining for the coronal reconstruction of the upper canine

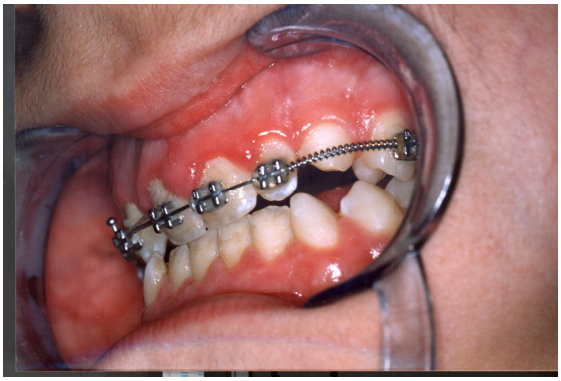


Fig. 5.4.4. The crown of the upper left primary canine was reshaped with adhesive filling technique.

5.4.2. Discussion

Congenitally missing permanent canine is an uncommon form of tooth agenesis with unknown aetiology (Lombardo *et al.* 2007). Frequently it occurs with other developmental deficiencies, such as hypo- or hyperdontia, and persisting primary canines. Several studies focused on twins or other family members suggest a specific autosomal character (Ulrich 1989, Lombardo *et al.* 2007). In the presented case the younger brother, described above, presented bilateral upper permanent canine ectopia, talon cusp and hypodontia of permanent teeth. Clinical implications of permanent canine agenesis are severe and early diagnosis is relevant. In young patients orthodontic therapy is preferred for space opening as preprosthetic therapy and also in cases of implant application (Leong and Calache 1999). In the presented case the management option was the most appropriate for the family at the time of presentation. The space opening with a coil spring made the aesthetical crown reconstruction with adhesive technique possible. The patient chose the prosthetic solution with resin bonded bridge (Maryland bridge) for replacement of the missing upper lateral incisor and was referred to the Prosthetic Department for further treatment.

6. Conclusions and new achievements of the present work

6.1. The findings of the present work are in agreement with the linguistic evidence that shows Hungarian ancestors belonged to the Finno-Ugrian family of people whose habitants extended from the Baltic to the middle Urals, and, from where, on the east-west migration route, they came to settle in the Carpatian Basin in 896 AD, mixing with people living there during the previous millennium (Szentpéteri 1996, Macartney 1962, Török 1962).
In the present work, for the first time in Hungary, the prevalence data of accessory tooth cusps in the contemporary population was compared with similar data from the ancestral population;

6.2. The majority of dental anomalies of developing dentition are numerical anomalies. Supernumerary teeth or hyperdontia describes an excess in tooth number. The prevalence of hyperdontia in permanent dentition is reported to lie between 1 and 3%.

The prevalence data of hyperdontia and hypodontia was determined and compared with international data for the first time in our country for 6- to 18-year-old patients;

6.3. Congenitally agenesis of permanent canines is uncommon and rare developmental anomaly of the human dentition. Its isolated or combined form can cause several problems such as: malocclusion, aesthetical and functional deficiencies. Further investigations are needed to help answering the questions raised by the distribution and racial differences in its occurrence.

For the first time the prevalence of congenitally missing permanent canines in young Hungarians was evaluated and compared with international data;

6.4. The maxillary canine is second only to the lower third molar in its impaction prevalence. Even detected at early ages, it often requires a complex multidisciplinary treatment, involving surgery, orthodontic treatment, prosthetics and implantology.

For the first time in Hungary the prevalence of impacted permanent canine was evaluated in correlation with the following orthodontic treatment;

6.5. The results of early prosthetic treatment of young HED patients are: significant improvements in speech, masticatory function and facial aesthetics. These contribute to the development of normal dietary habits and the improved and more rapid social integration of the affected children.

During treatment of patients with HED, early prosthetic treatment consisting of oral rehabilitation of two 3 year old patients was successfully achieved by application for the first time of complete dentures at such a young age in our country.

The complex, surgical and orthodontic, treatment of a special case of supernumerary permanent teeth was presented.

7. Summary

Developmental dental anomalies are an important category of dental symptomatology. Their incidence and degree of expression can provide important information for phylogenic and genetic studies and helps the understanding of variations within and among populations. The prevalence studies of the present work were evaluations on young patient groups of different ages who presented for paedodontic and/or orthodontic treatment at the Department for Paedodontics and Orthodontics, Semmelweis University Budapest. Chi-square test was used for statistical analysis.

Among the morphological characteristics the Carabelli and the talon cusps are expressed in several degrees and different frequencies between humans, thus being useful in comparing and characterizing populations. The aetiology of both remains unknown. Genetic and exogenous factors may combine to determine their phenotypical appearance. A Carabelli cusp is more common in Europeans than Mongoloids, while talon cusp is less common in Caucasians. In the present work the incidence and degree of expression of both Carabelli and talon cusps were studied in a contemporary Hungarian population consisting of 600 children aged 7 to 18 years. Their appearance and characteristics were evaluated from an anthropological point of view by comparison with the prevalence of the two cusp types on teeth from 147 skulls dating from the 11^{th} century Árpád-era. A significant difference between the contemporary and the 11^{th} century group was found for both morphological anomalies, for the Carabelli cusp: $p<0.01$; for the talon cusp: $p<0.001$. The data are in agreement with linguistic evidence that shows the ancestors of present day Hungarians belonged to the Finno-Ugrian family of people whose habitats extended from the Baltic to the middle Urals, and, from where, on the east-west migration route, they came to settle in the Carpathian Basin in the 9^{th} century, mixing with people living there during the previous millennium.

The majority of dental anomalies of developing dentition are numerical anomalies. Supernumerary teeth or hyperdontia describes an excess in tooth number. The prevalence of hyperdontia in permanent dentition is reported to lie between 1 and 3% and this form of anomaly is considerably rarer in the primary than permanent dentition. The aetiology of this anomaly is unknown, and several theories have been suggested. The data on the prevalence of hypodontia or CMT reveal great variations in both the primary and the permanent dentition. The aim of the present work is to fill the gap caused by the absence of data for the young Hungarian population by determining the prevalence of hyperdontia and hypodontia in the permanent dentition of the 6- to 18-year-old age group. For this purpose the OPGs of 2219

orthodontic patients were examined. The prevalence of hyperdontia was 1.53%, that of hypodontia 14.69%. The case reports in the recent literature state that while there are an increasing number of implants and tooth germ transplants, hyper-and hypodontia are mainly treated by orthodontics and restorative dentistry. One of the reasons for this is the fact that supernumerary teeth can cause clinical problems such as failure of eruption, displacement or rotation, crowding etc. The purpose of the case report related to the tuberculate and odontoma type supernumerary teeth shown in the present work was to describe the importance of early surgical and orthodontic treatment during mixed dentition to be able to prevent or minimize further complications.

Hypodontia of the primary and permanent dentition, associated with hypoplasia of the alveolar bone structures, is the second most frequently occurring oral symptom accompanying the large and complex nosological group of congenital diseases, such as EDs. The number of missing teeth varies, with higher incidence in the lower jaw. In the present work the early prosthetic oral rehabilitation of 2 young male patients with a hypohydrotic form of ED is presented, both cases associated with severe anodontia in primary dentition. Prosthetic treatment was recommended beginning at the age of 3. It contributes to a normal physiological development of the children, improves the function of the stomatognathic system, and helps HED children's integration into their social environment.

Permanent canine agenesis is a rare form of dental anomaly. It occurs more commonly in Asiatic population and was also occasionally described in primary dentition. In the present work the prevalence and distribution of PCA is analysed in 4221 6- to 8-year-old healthy patients who presented for treatment over a period of 10 years. The findings show a prevalence of 0.29%.

Among tooth malpositions the impacted upper canine shows a very high prevalence. In the present work data relating to 1858 eleven to eighteen-year-old children presented for treatment at the Department for Paedodontics and Orthodontics, Semmelweis University Budapest. over a period of 10 years were analysed to calculate the prevalence of impacted or retentioned permanent upper canines. Prevalence of 5.43% was found and 96.92% of the totality of administered treatment methods consisted of both surgical exposure and orthodontic treatment. Further, in 40.91% of the treated cases extraction of the correspondent upper first premolar was needed, and in 3.03% spontaneous occlusion of the impacted canine was established following premolar extraction.

It was the objective of the present work to provide new information concerning the prevalence of hypo- and hyperdontia, Carabelli and talon cusps, rare forms of CMT like canine agenesis

and frequent malpositions, such as upper permanent canine impaction. The aim was also to present treatment possibilities during the developing dentition period considering that developmental dental anomalies can be challenging to manage clinically and their effective solution requires careful multidisciplinary planning, with input from a paedodontist, orthodontist, restorative dentist, an oral surgeon and, occasionally a speech therapist.

8. References

1. **Aasheim B, Ogaard B.** *Hypodontia in 9-year-old Norwegians related to need of orthodontic treatment.* Scand J Dent Res 1993; 101: 256-260;
2. **Abadi BJ, Kimmel NA, Falace DA.** *Modified overdentures for the management of oligodontia and developmental defects*. ASDC J Dent Child 1982;49:123-6.
3. **Adler-Hradeczky C, Polczer MG.** *Das Geschlechtsunterschied in der Frequenz der Dystopie des oberen Eckzahnes.* Dtsch Zahnärztl Z 1960; 15: 732-736.
4. **Altug-Atac A T, Erdem D**. *Prevalence and distribution of dental anomalies in orthodontic patients*. Am J Orthod Dentofac Orthoped 2007; 131: 510-514;
5. **Alvesalo N, Nuutila M, Portin P.** *The cusps of Carabelli, occurrence in first upper molars and evaluation of its heritability.* Acta Odontol Scand 1975; 33:191-197.
6. **Andlaw RJ, Rock WR.** *A manual of Paediatric Dentistry.* Churchill Livingstone, Fourth ed. London, 1996; p. 151.
7. **Babu V, Nagesh KS, Diwakar NR,** *A rare case of hereditary multiple impacted normal and supernumerary teeth.* J Clin Pediatr Dent 1998; 23: 59-61;
8. **Baccetti T.** *A controlled study of associated dental anomalies*. Angle Orthod 1998; 68:267-74.
9. **Baergen R, Baergen C.** *Paternalism, risk and patient choice.* J Am Dent Assoc 1997; 128: 481-484.
10. **Bailit H L**. *Dental variations among populations. An anthropological view.* Dent Clin North Am 1975;19: 125-139;
11. **Bakody R.** *Cases of isolated aplasia of upper permanent cuspids.* Fogorv Szle 1974; 67(7): 198-200;
12. **Bakody R**. *Aplasia of the permanent cuspids.* Fogorv Szle 1975; 68(2): 54-58;
13. **Bakody R, Balaton P**. *Isolated aplasia of the upper cuspids and its orthodontic management.* Fogorv Szle 1992; 85(9): 271-273
14. **Bass TP.** *Observation on the misplaced upper canine tooth.* Dent Pract 1967; 18: 25-33.
15. **Beer de, G R**. *Embryos and Ancestors*. Clarendon Press. Oxford, 1951;pp.58-59
16. **Becktor KB, Becktor JP, Keller EE**. *Growth analysis of a patient with ectodermal dysplasia treated with endosseous implants: a case report.* Int J Oral Maxillofac Implants 2001;16:864-74.
17. **Bergström K** *An orthopantomographic study of hypodontia, supernumeraries and other anomalies in school children between ages of 8-9 years. An epidemiological study*. Swedish Dent J 1977;1: 145-157
18. **Berkoitz BK, Thompson P.** *Observation on the aetiology of supernumerary upper incisors in the albino ferret (Mustela putorius).* Arch oral Biol 1973; 18(4): 457-463.
19. **Bishara SE**. *Impacted maxillary canines: a review.* Am J Orthod Dentofacial Orthop 1992; 101:159-71.
20. **Bonilla ED, Guerra L, Luna O.** *Overdenture prosthesis for oral rehabilitation of hypohidrotic ectodermal dysplasia: a case report.* Quintessence Int 1997; 28:657-65.
21. **Bolan M, Gerent Patry Nuns AC, de Carvalho Rocha MJ, de Luca Canto G.** *Taln cusp : report of a case.* Quintessence Int 2006; 37(7): 509-514.
22. **Boros S.** *Fogászati Pathológia.* Medicina Könyvkiadó, Budapest, 1961 pp. 10-11.
23. **Bótyik M, Elisher Z, Harmatis S** *Aplasia of all 4 permanet canine teeth*. Fogorv Szle 1977; 70(3): 81-82
24. **Brook A H**. *A unifying aetiological explanation for anomalies of human tooth number and size.* Arch Oral Biol 1984; 29: 373-378;
25. **Buenviaje TM, Rapp R.** *Dental anomalies in children a clinical and radiographic survey.* J Dent Child 1984; 51:42-46.
26. **Burzynski N J, Escobar V H.** *Classification and genetics of numeric anomalies of dentition.* Birth defects original article series 1983; 19(1): 95-106;
27. **Butler P M**. *Studies of the mammalian dentition. Differentiation of the post-canine dentition.* Proceed Zoologic Soc London 1939;109B: 1-36;
28. Buyse ML. *Birth defects encyclopedia*. St. Louis: Blackwell Publishing. 1990. p. 597-8

29. **Cabov T, Tomljenovi K, Legovi A, Kovac Z, Peri B, Joki D**. *A case of canine hypodontia in an early Croatian cemetery Strance-Gorica.* Collegium Antropologicum 2006; 30: 443-446;
30. **Cakur B, Dagistan S, Özkan M, Bilge M.** *Nonsyndromic Oligodontia in Permanent Dentition: Three Siblings.* Internet J Dent Science 2006; Vol.3, Nr.2.
31. **Camilleri J.** *A case of bilateral supplemental maxillary central incisors.* Int J Paed Dent 1976;13:57-61
32. **Chawla HS, Tewari A, Gopalakrishnan NS**. *Talon cusp - a prevalence study*. J Indian Soc Pedodont Prev Dent 1983; 1:28-34.
33. **Chen RJ, Chen HS.** *Talon cusp in primary dentition.* Oral Surg Oral Med Oral Pathok 1986; 62(1): 67-72.
34. **Cho S**. *A case of bilateral congenitally missing mandibular permanent canines.* Hong Kong Dent J 2004;1: 96-97;
35. **Cho S, Lee C**. *Hypodontia involving only mandibular permanent canines: Report of six cases.* J Dent Child 2004; 71(3): 197-200;
36. **Cho S, Lee C, Chan J C**. *Congenitally missing maxillary permanent canines: report of 32 cases from an ethnic Chinese population*. J Dent Child 2004; 14(6): 446-450.
37. **Clouston HR.** *The major forms of hereditary ectodermal dysplasia*. Can Med Assoc J 1939;40:1-7.
38. **Cozza P, Lagana G, Mucedero M.** *Early diagnosis and treatment of supplemental mandibular tooth: Report of a case.* J Dent Child 2002;69:180-183
39. **Dachi SF, Howell FV.** *A survey of 3874 routine full mouth radiographs.* Oral Surg Oral Med Oral Pathol 1961; 14: 1165-1169.
40. **Dahlberg AS.** *Analysis of American Idian dentition. In: Prothwell D R (ed.) Dental anthropology.* Pergamon Press, Oxford. 1963; pp 149-178.
41. **Dahlberg, A A** . *The changing dentition of man*. J Am Dent Assoc 1945; 32: 676-690
42. **Dahlberg A A**. *The dentition of the American Indian. In: W. S. Laughlin. (ed.), Papers on the Physical Anthropology of the American Indians.* The Viking Fund, New York, 1949; pp. 138-176.
43. **Davis PJ, Rook AH**. *The presentation of talon cusp: diagnosis, clinical features, associations and possible aetiology.* British Dent J 1985; 159:84-88.
44. **Davis P J**. *Hypodontia and hyperdontia of permanent teeth in Hong Kong schoolchildren.* Comm Dent Oral Epidem 1987; 15: 218-220.
45. **Di Biase DD.** *Midline supernumeraries and eruption of the maxillary central incisor.* Dent Pract Dent Rec 1969; 20(1): 35-40.
46. **Dietz VHA.** Com*mon dental morphotropic factor: the Carabelli's cusp*. J Am Dent Assoc 1994; 31: 784-789.
47. **Dolder E**. *Deficient dentition.* Statistical survey. Dental record 1973; 57: 142-143.
48. **Duncan BR, Dohner VA, Preist JH.** *Gardner's syndrome: need for early diagnosis.* J Pediatr 1968; 72:497.
49. **Dyson JE.** *Prosthodontics for children*. In: Wei SHY, editor. Pediatric dentistry and orthodontics: Total patient care. Philadelphia: Lea & Febiger; 1988. p. 259-74.
50. **Egermark-Eriksson I, Lind V.** *Congenital numerical variation in the permanent dentition. Sexdistribution of hypodontia and hyperodontia.* Odontologiskrevy 1971; 22:309-315.
51. **Endo T, Ozoe R, Yoshino S, Shimooka S**. *Hypodontia patterns and variations in craniofacial morphology in Japanese orthodontic patients*. Angle Orthodontist; 2006;76(6): 996-1003.
52. **Ericson S, Kurol J.** *Longitudinal study and analysis of clinical supervision of maxillary canine eruption.* Community Dent Oral Epidemiol 1986; 14:172-176.
53. **Fekonja A.** *Hypodontia in orthodontically treated children.* Europ J Orthod 2005; 25: 457-460.
54. **Ferguson JW.** *Management of the unerupted maxillary canine.* Br Dent J 1990; 169: 11-17.
55. **Firu P.** *Stomatologie infantila*. Editura Didactica si Pedagogica, Buduresti, 1983. p.109.
56. **Foster TD, Taylor GS.** *Characteristics of supernumerary teeth in the upper central incisor region.* Dent Pract Dent Rec 1969;20:8-12.

57. **Franchi L, Branchi R, Tollaro I.** *Craniofacial changes following early prosthetic treatment in a case of hypohidrotic ectodermal dysplasia with complete anodontia.* ASDC J Dent Child 1998;65:116-21.
58. **Fukuta Y, Totsuka M, Takeda Y, Yamamoto** c **H.** *Congenital absebce of the permanent canines: a clinico-statistical study.* J Oral Science 2004; 46: 247-252.
59. **Gallas MM, Garcia A.** *Retention of permanent incisors by mesiodens: a family affair*. British Dent J 2000; 188: 63-64.
60. **Garvey MT, Barry HJ, Blake M.** *Supernumerary teeth - an overview of classification, diagnosis and management.* J Can Dent Assoc 1999; 65: 612-616.
61. **Gianniou E, Kouthikou T H, Sarikou E, Dimitrakopoulos I.** *Incidence and expression of Carabelli's cusp in a contemporary Greek population.* Stoma 2000; 28:123-132.
62. **Gouse PH, Lee GTR.** *The mode of inheritance of Carabellis' trait*. Human Biol 1971; 43:69-91.
63. **Grover PS, Lorton L.** *The incidence of ureruupted permanent teeth and related clinical cases.* Oral Surg Oral med Oral Pathol 1985; 59: 420-429.
64. **Guckes AD, Scurria MS, King TS, McCarthy GR, Brahim JS.** *Prospective clinical trial of dental implants in persons with ectodermal dysplasia.* J Prosthet Dent 2002; 88:21-25.
65. **Hallet G E, Weyman J**. *Fourteen cases of congenital absence of canines*. British Dental Journal 1954; 97: 228-230.
66. **Hassanali J.** *Incidence of Carabelli's trait in Kenyan Africans and Asians*. Am J Physic Anthropol 1982; 59: 317-319.
67. **Haselden K, Hobkirk J A, Goodman J R, Jones S P, Hemmings K W** 2001 *Root resorption in retained deciduous canine and molar teeth without permanent successors in patients with severe hypodontia.* Int J Paediatric Dent 11: 171-178.
68. **Hattab FN, Yassin OM, Rawashdeh MA.** *Supernumerary teeth: Report of three cases and review of the literature.* ASDC J Dent Child 1994;61:38-93.
69. **Hattab FH, Yassin OM, Al-Nimri KS.** *Talon cusp in permanent dentition associated with other dental anomalies: review of literature and reports of seven cases.* ASDC J Dent Child 1996; 6:368-376.
70. **Hedge S, Kumar BRA.** *Mandibular talon cusp: report of two rare cases.* Intl J Paed Dent 1999; 9:303-306.
71. **Henderson HZ**. *Talon cusp: a primary or a permanent incisor anomaly*. J Indiana Dent Assoc 1997; 56:45-46.
72. **Hokari S, Inoue N, Inoue H, Okumura Y.** *Statistical observation on congenital missing of teeth in our university students*. Nihon Koku Shindan Gakkai Zasshi 2000;13: 228-232.
73. **Huggare J.** *Congenital aplasia of four permanent cuspids. A case report.* Proceed Finnish Dent Soc 1984; 80: 257-259.
74. **Hsu JW, Tsai P, Ferguson D.** *Logistic analysis of shovel and Carabelli's tooth traits in a Caucasoid population.* Forensic Science Intl 1997; 89:65-74.
75. **Imirzalioglu P, Uckan S, Haydar SG.** *Surgical and prosthodontic treatment alternatives for children and adolescents with ectodermal dysplasia: a clinical report.* J Prosthet Dent 2002;88:569-72.
76. **Jaskoll T, Zhou YM, Trump G, Melnick M.** *Ectodysplasin receptor-mediated signaling in essential for embryonic submandibular salivary gland development.* Anat Rec A Discov Mol Cell Evol Biol 2003; 271: 322-331.
77. **Johnson EL, Roberts MW, Guckes AD, Bailey LJ, Phillips CL, Wright JT**. *Analysis of craniofacial development in children with hypohidrotic ectodermal dysplasia.* Am J Med Genet 2002;112:327-34.
78. **Jorgenson RJ.** *Clinicians' view of hypodontia*. J Am Dent Assoc 1980;101: 283-286.
79. **Kanappan JG, Swaminathab S.** *A study on dental morphological variation. Tubercle of Carabelli.* Indian J Dent Res 2001; 12:145-149.
80. **Kieser JA, Van Der Merwe CA** . *Classificatory reliability of the Carabelli trait in man.* Archives Oral Biol 1984; 29: 795-801.
81. **Kraus BS.** *Carabellis' anomaly of the maxillary teeth.* Am J Human Genet 1951; 3:348-355.

82. **Larmour CJ, Mossey PA, Thind BS, Forgie AH, Stirrups DR.** *Hypodontia – a retrospective review of prevalence and etiology. Part I.* Quintessence Int 2005; 36(4):263-270.
83. **László S** *3 variants of aplasia of the permanent cuspid*. Fogorv Szle 1978; 71(1): 29-31.
84. **Lekholm U.** *The use of osseointegrated implants in growing jaws.* Int J Oral Maxillofac Implants 1993; 8: 243-244.
85. **Leong P, Calache H.** *Bilateral congenitally missing maxillary canines. A case report.* Aust Dent J 1999; 44(4): 279-282.
86. **Levin LS.** *Dental and oral abnormalities in selected ectodermal dysplasia syndromes*. Birth Defects Orig Artic Ser 1988; 24:205-27.
87. **Levine N.** *The clinical management of supernumerary teeth.* J Can Dent Assoc 1961; 28:297-303.
88. **Lombardo C, Barbato E, Leonardi R** *Bilateral maxillary canines agenesis: a case report and a literature review. (Review).* Europ J Paedod Dent 2007; 8: 38-41.
89. **Lum Y M, Lim S T** *Four cases of congenitally missing permanent cuspids*. Singapore Dent J 1976; 2: 49-51.
90. **Macartney CA.** *Hungary. A short history.* Edinburgh University Pres, Edinburg, pp. 1-15.
91. **Machen DE.** *Legal aspects of orthodontic practice: risc management concepts. The impacted canine.* Am J Orthod Dentofacial Orthop 1989; 96: 270-270.
92. **Mader CL.** *Talon cusp.* J Am Dent Assoc 1981; 103: 244-246;
93. **Mason C, Rule DC, Hopper C.** *Multiple supernumeraries: the importance of clinical and radiographic follow-up.* Dentomaxillofac Radiol 1996;25:109-113.
94. **Mavrodisz K, Budai M, Tarján I.** *The prevalence of talon csp in patients aged 7-18.* Fogorv Szle 2003; 96(6): 257-259.
95. **McKibben DR, Brearly LJ.** *Radiographic determination of the prevalence of selected dental anomalies in children.*ASDC J Dent Child 1971; 28(6);390-398.
96. **McNamara CM, Foley TF, Wright GZ, Sandy JR**. *The management of premolar supernumeraries in three orthodontic cases.* J Clinic Pediatric Dent 1997; 22: 15-18.
97. **McNamara CM, Garvey MT, Winter GB.** *Root abnormalities, talon cusps, dens invaginati with reduced alveolar bone levels: case report.* Int J Paed Dent 1998; 8:41-45.
98. **McSherry PF.** *The ectopic maxillary canine: A review.* Br J Orthod 1998; 25: 209-216.
99. **McVaney TP, Kalkwarf KL**. *Misdiagnosis of an impacted supernumerary tooth from a pantographic radiograph.* Oral Surg Oral Med Oral Pathol 1976;41:678-681.
100. **Melamed Y, Barkai G, Frydrnan M.** *Multiple supernumerary teeth (MSNT) and Ehlers-Danlos syndrome (EDS): a case report.* J Oral Pathol Med 1994;23:88-91.
101. **Mellor JK, Ripa LW.** *Talon cusp: a clinically significant anomaly.* Oral Surgery 1970; Ramos et al. 1995). 29:225-228.
102. **Mitchell AC, Grant AA.** *The effect of complete dentures on the development of speech articulation in children.* J Dent 1976;4:175-82.
103. **Mitchell L, Mitchell D.** *Abnormalities of tooth number,* In: Mitchell L, Mitchell D. Oxford Handbook of Clinical Dentistry. 3rd ed. New York: Oxford University Press 1992; pp. 68.
104. **Mitchell WH.** *Case report.* Dental Cosmos 1892; 34:10-36.
105. **Moore SR, Wilson DF, Kibble J**. *Sequential development of multiple supernumerary teeth in the mandibular region - a radiographic case report.* Int J Paed Dent 2002;12:143-145.
106. **Moss JP.** *The unerupted canine.* Dent Pract 1972; 22: 241-248.
107. **Muller TP, Hill IN, Petersen AC, Blayney JR** : *A survey of congenitally missing permanent teeth.* J Am Dent Assoc 1970; 81:101-107.
108. **Munns D.** *Unerupted incisors*. British J Orthod 1981;8:39-42.
109. **Nordgarden H, Jensen JL, Storhaug K.** *Reported prevalence of congenitally missing teeth in two Norwegian counties.* Comm Dent Health 2002; 19: 258-261.
110. **O'Dwyer MR, Renner RP, Fergusen FS.** *Overdenture treatment – One aspect of the team approach for the EEC syndrome patient.* J Pedod 1984;8:192-205.
111. **Palomino H, Chakraborty R, Rothlammer F.** *Dental morphology and population diversity.* Human Biol 1977; 46:6-7.

112. **Pigno MA, Blackman RB, Cronin RJ Jr, Cavazos E.** *Prosthodontic management of ectodermal dysplasia: a review of the literature.* J Prosthet Dent 1996; 76: 541-545.
113. **Pirinen S, Thesleff I.** *Development of the dentition. In: Thilander B, Ronning O (ed) Introduction to Orthodontics.* Lic Forlag, Stockholm, 1995; pp. 41-43.
114. **Power SM, Short MB.** *An investigation into the response of palatally displaced canines to the removal of deciduous canines and an assessment of factors contributing to favourable eruption.* British J Orthod 1993; 20:217-213.
115. **Priolo M, Lagana C.** *Ectodermal dysplasia: a new clinical-genetic classification*. J Med Genet 2001;38:579-585.
116. **Rajab LD, Hamdan MAM.** *Supernumerary teeth: review of the literature and a survey of 152 cases.* Int J Paed Dent 2002; 12:244-254.
117. **Ramaraj S, Mirza Y.** *Bilateral congenitally missing mandibular canines with supplementary lower incisor. A case report.*Saudi Dent J 1995; 7(2):108-110.
118. **Ramos V, Giebink DL, Fisher JG, Christensen LC.** *Complete dentures for a child with hypohidrotic ectodermal dysplasia: a clinical report.* J Prosthet Dent 1995; 74: 329-331.
119. **Rayne J.** *The unerupted maxillary canine.* Dent Pract Dent Rec 1969; 19:194-204.
120. **Richardson A, Deussen FF.** *Facial and dental anomalies in cleidocranial dysplasia: a study of 17 cases.* Int J Paed Dent 1994; 4: 225-231.
121. **Richardson G, Russell KA.** *A review of impacted permanent maxillary cuspids – diagnosis and prevention.* J Can Dent Assoc 2000; 66(9): 497-501.
122. **Riekman GA, el Badrawy HE.** *Effect of premature loss of primary maxillary incisors on speech.* Pediatr Dent 1985;7:119-22.
123. **Rizzuti N, Scotti S**. *A case of hyperdontia with twenty-two supernumeraries: its surgical-orthodontic treatment.* Am J Orthod Dentofac Orthoped 1997; 111: 471-480.
124. **Robertson NRE.** *Three cases of congenitally missing permanent cuspids*. Dental Digest 1962; 68: 68-69.
125. **Rose J S**. A survey of congenitally missing teeth, excluding third molas, in 6000 orthodontic patients. The Dental practitioner and dental record 1966; 17(3): 107-114.
126. **Rushman H, Meon R.** *Talon cusp in Malaysia.* Australian Dent J 1991; 36:11-14.
127. **Saksena SS, Bixler D.** *Facial morphometrics in the identification of gene carriers of X-linked hypohidrotic ectodermal dysplasia.* Am J Med Genet 1990;35:105-14.
128. **Schalk van der Weide Y, Beemer F A, Faber J A J, Bosman F**. *Symptomatology of patients with oligodontia. Journal* of Oral Rehabilitation 1994; 21: 247-261.
129. **Schopf P.** *Curriculum für Kieferorthopädie.* Band 1 Quintessenz, Berlin, 1991; pp. 38-39.
130. **Segura-Egea JJ, Jiménez-Rubio A, Velasco-Ortega E, Ríos-Santos JV.** *Talon cusp causing occlusal trauma and acute apical periodontitis: report of a case.* Dent Traumatol 2003; 19(1): 55-59.
131. **Shah RM, Boyd MA, Vatril TF.** *Studies of permanent tooth anomalies in 7886 Canadian individuals.* J Can Dent Assoc 1978; 44: 262-264.
132. **Sharma A** *A rare non-syndrome case of concomitant multiple supernumerary teeth and partial anodontia.* J Clin Pediat Dent 2001; 25(2): 167-169.
133. **Shapira Y, Kuftinec MN**. *Early diagnosis and interception of potential maxillary canine impaction.* J Am Dent Assoc 1998; 129:1450-1454.
134. **Shaw RM.** *Prosthetic management of hypohidrotic ectodermal dysplasia with anodontia. Case report.* Aust Dent J 1990;35:113-6.
135. **Sinkovits V, Polczer MG.** *Die Häufigkeit retinierter Zähne.* Dtsch Zahnärztl Z 1964; 19: 389-396.
136. **Silverman N E, Ackerman J L** *Oligodontia:a study of its prevalence and variations in 4032 children.* J Dent Child 1979; 46: 470-477.
137. **Szepesi M, Nemes J, Kovalecz G, Alberth M**. *Prevalence of hypodontia in 4-18-year-old children in Department of Paediatric Dentistry, Faculty of Dentistry, University of Debrecen from 1999 to 2003.* Fogorv Szle 2006; 99(3): 115-119.
138. **Stellzig A, Basdra EK, Komposch G.** *Mesiodentes: incidence, morphology etiology.* J Orofac Orthoped 1997; 58: 144-146.

139. **Szentpéteri J.** *Prehistory. The age of Hungarian conquest. From: Emese Saga.* Encyclopedia Humana Hungarica 01. Encyclopaedia Humana Association, Budapest, pp. 1-4 (CD-ROM).
140. **Takashi O, Ryosuke I, Kenro M, Shizou S.** *The prevalence of developmental anomalies of teeth and their association with tooth size in the primary and permanent dentitions os 1650 Japanese children.* Int J Paed Dent 1996; 6: 87-94.
141. **Taylor TD, Hayflick SJ, McKinnon W, Guttmacher AE, Hovnanian A, Litt M, *et al.*** *Confirmation of linkage of Clouston syndrome (hidrotic enamel dysplasia) to 13q11-q12.1 with evidence for multiple independent mutations.* J Invest Dermatol 1998;111:83-85.
142. **Thilander B, Jakobsson SO.** *Local factors in impaction of maxillary canines*. Acta Odontol Scand 1968; 26:145-68.
143. **Török Gy.** *Die Bewohner von Halimba im 10. und 11. Jahrhundert.* Archeologia Hungarica: 1962; Series nova: 39:111-124.
144. **Ulrich K.** *Isolated canine aplasia in monizygotic twins.* Fortschr Kieferorthop 1989; 50: 415-422.
145. **Warford Jr JH, Granghi RK, Tira DE.** *Prediction of maxillary canine impaction using sector and angular measurement.* Am J Orthod Orthofacial Orhtop 2003; 124: 651-655.
146. **Zilberman Y, Cohen B, Becker A.** *Familial trends in palatal canines, anomalous lateral incisors, and related phenomena.* Eur J Orthod 1990; 12:135-139.

KÖSZÖNETNYILVÁNÍTÁS

Köszönöm édesanyámnak, aki mindvégig mellettem állt, és segített célkitűzéseim elérésében; köszönöm családomnak a támogatást és a türelmet;
köszönöm Prof. Dr. med habil Tarján Ildikónak, Prof. Dr. med habil Nagy Katalinnak, Dr. med habil Gábris Katalinnak, Prof. Dr. med habil Vajó Zoltánnak, és Fiona Hatelynek, akik szakmailag és barátilag kitartóan támogattak értékes tanácsaikkal, kritikáikkal, és akik nélkül ez a dolgozat nem jött volna létre.

ACKNOWLEDGEMENT

I thank my mother who always supported my scientific and personal goals.
I thank my family for the support and patients during the finalization of my work.
I would like to thank Prof. Dr. med habil Ildikó Tarján, Prof. Dr. med habil Katalin Nagy, Dr. med. habil Katalin Gábris, Prof. Dr. med habil Zoltán Vajó, and Fiona Hately for their valuable support, persistent help and advice that was so significant in the writing of the present dissertation.