# Oligodontia

## A clinical, radiographic and genetic evaluation

**Y. Schalk-van der Weide**

# Oligodontia

*- A clinical, radiographic and genetic evaluation -*

**Yvonne Schalk - van der Weide**

## Stellingen behorende bij het proefschrift:

## Oligodontia: A clinical, radiographic and genetic evaluation

1 Het is belangrijk onderscheid te maken tussen geïsoleerde oligodontie en oligodontie als onderdeel van een syndroom.

2 Hoe meer gebitselementen niet zijn aangelegd, hoe groter de reductie in vorm en grootte van de wel aangelegde gebitselementen.

3 Als men in één generatie van een geslacht kenmerken van oligodontie aantreft moet men bedacht zijn op kenmerken van oligodontie in een volgende generatie.

4 Extractie van melkelementen bij oligodontiepatiënten moet zorgvuldig worden afgewogen, daar het handhaven van deze elementen kan bijdragen aan het behoud van de processus alveolaris.

5 De tandarts is te vaak alleen geïnteresseerd in de gebitselementen die aanwezig zijn.

6 Het constateren van een verworven of aangeboren afwijking aan het (melk)gebit zonder het aan de patiënt mee te delen of verdere aktie te ondernemen is een kunstfout.

7 Oligodontiepatiënten staan nooit met hun mond vol tanden.

8 Kegeltanden zijn voor kinderen met oligodontie als een nachtmerrie waarin Dracula de hoofdrol speelt.

9 De kwantiteit en kwaliteit van stellingen bij een proefschrift zijn niet per definitie maatgevend voor de algemene ontwikkeling van de promovendus.

10 Er bestaat geen mooier ijs dan natuurijs.

11 Voor die wetenschappers voor wie het geluid van de radio een verstorende factor is, klinkt de stilte als muziek in de oren.

12 In de huidige muziek is het spreekwoord "Oost West Thuis Best" gedeformeerd tot "East West House Best".

13 De slogan van 1992 "Eén Europa" doet het ergste vermoeden als men daar één Joegoslavië tegen afzet.

Woerden, september 1992

RIJKSUNIVERSITEIT UTRECHT

# Oligodontia

*- A clinical, radiographic and genetic evaluation -*

# Oligodontie

*- Een klinische, röntgenologische en genetische evaluatie -*

(met een samenvatting in het Nederlands)

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aan de Rijksuniversiteit te Utrecht
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ingevolge het besluit van het College van Dekanen
in het openbaar te verdedigen
op dinsdag 1 december 1992 des namiddags te 2.30 uur.

door

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geboren op 9 juni 1965 te Breukelen

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# Chapter 1
# Introduction and aims of the study

## 1.1 Introduction

Oligodontia is usually circumscribed as the congenital missing of a large number of teeth. Oligodontia can occur isolated or as part of a syndrome. These two forms will be referred to as oligodontia/I (isolated oligodontia) and oligodontia/S (oligodontia as part of a syndrome). The main dental features of oligodontia are a reduction in the number of teeth, reduced size and form of the teeth, anomalies of the enamel and delayed eruption. These dental symptoms are characteristic for both patients with oligodontia/I and oligodontia/S. Besides these dental symptoms patients with oligodontia/S are characterized by anomalies of other organs and systems such as hypohidrosis, hypertrichosis and onychodystrophy.

The dental treatment of the patients with oligodontia is often complicated. This is not only due to the number of absent teeth but also to other associated dental anomalies and problems, such as a deep-set plica mentalis, and to psycho-social problems.

Because of the multidisciplinary problems - including psycho-social problems, problems in dental treatment and the possible association with syndromes - the dental practitioner confronted with these patients often refers them to special centres such as Departments of Oral-Maxillofacial Surgery, Prosthodontics and Special Dental Care.

## 1.2 Relevance of the problem

From dental clinical experience we know that congenitally missing teeth or oligodontia is not uncommon. However, a prevalence of congenitally missing teeth in the Netherlands is not known. No real figures can be given, therefore, concerning the number of patients with which a dental practitioner will be confronted with during his or her years in general practice.

To the patient and the parents two items are most important. First their attention is directed towards the aesthetical problems associated with the anomaly. Due to the missing of a large number of teeth, the patient has an abnormal facial appearance. Diastemas and abnormally shaped teeth make the patient feel uncomfortable. Children experience their abnormal facial appearance as very unpleasant, particularly when other children laugh at them and make jokes about their abnormally shaped teeth. Secondly, the patients and/or the parents are worried about the next generation, i.e. is the anomaly inherited and what can be expected in the next generation. Information is needed concerning dental therapy and the influence of environmental and/ or genetic factors to answer these questions.

The dental practitioner, who is confronted with patients with oligodontia, should be able to inform these patients about the character and the severity of the disorder. To do so three important questions must be asked:

a) How can a correct diagnosis be made?
b) Should the patient be referred?
c) Which type of dental therapy is suitable?

To be able to answer these questions the dental practitioner needs information about the symptomatology of oligodontia and about dental therapy.

*Diagnosis / Genetic counselling*

A correct diagnosis of oligodontia can only be derived when the dental practitioner has sufficient knowledge of symptoms and signs associated with oligodontia, both oral and extra-oral characteristics. Only a few syndromes can be recognised by their specific patterns of missing teeth. Most syndromes can only be diagnosed after additional, sometimes multidisciplinary investigations. Knowledge of the symptoms and patterns of symptoms or patterns of missing teeth helps in making an early diagnosis, which is important for dental treatment and genetic counselling. For genetic counselling, a correct diagnosis is a prerequisite.

*Dental symptoms and therapy*

The occurrence of the dental symptoms, as described, influences the choice of dental therapy. Therefore, knowledge of these symptoms is important.

The time of eruption, for example, influences the planning of dental treatment. It can also be important in making a diagnosis, particularly when eruption appears to be delayed. The length of the teeth is of importance when considering orthodontic therapy. The loading of a prosthetic construction depends, amongst other things, on the length of the teeth. Reduced length can lead to an unfavourable crown-root ratio. Furthermore, in cases with small conical crowns, bridgework is likely to fail rapidly.

## 1.3 Aims of the study

Up to now, information about symptoms occurring in Dutch patients with oligodontia had to be obtained from studies done in other countries. To the author's knowledge, Dutch patients with oligodontia have never been the subject of extensive studies.

The aim of this study was to define the symptoms occurring in a population of Dutch patients with oligodontia and to contribute to the knowledge of how the disorder is inherited. This knowledge will enable the dental practitioner to make the diagnosis of congenitally missing teeth and inform the patient about the character and severity of his/her disorder and the possibility of genetic consequences.

The following questions were posed:

*Symptomatology*

1. Which symptoms are present in a population of Dutch patients with oligodontia?
1a. Do the teeth of this population show reductions in size and/or form of the crown or root?
1b. Is the dental age of this population of patients retarded?
2. Are there correlations between extra-oral symptoms and patterns of missing teeth?

*Etiology*

1. If the anomaly is familiar, what is the possible mode of inheritance?

*Practical applications*

1. Which variables are important for the dental practitioner in order to distinguish between oligodontia/I and oligodontia/S?

## 1.4 Operational definitions and abbreviations

Definitions as used in this study will be given in this section.

*Oligodontia*

In this study, oligodontia is defined as follows:

> The congenital missing of six or more teeth, excluding the third molars.

Witkop (1989) stated that the use of the term oligodontia or hypodontia is a secondary consideration as long as the terms used are defined. In literature there is no consensus on the definition of oligodontia or hypodontia (Chapter 2).

The reasons for choosing the definition used in the present study were as follows: a) in those patients, aesthetic and functional disturbances can be observed, b) it ensures a limitation of the group, c) this definition holds with the definition of severe hypodontia defined by other authors (Whisth et al., 1974; Hobkirk and Brook, 1980).

*Tooth morphology*

In this study the discussion on tooth morphology is divided into two parts, the size of the teeth and the morphology of the teeth. When discussing the morphology of the teeth in this study, the form and or shape of teeth is meant. Definitions are given in Table 1.1.

**Table 1.1** *Definition of tooth morphology.*

* Size of the teeth:
  > mesiodistal and labiolingual dimension of the crown
  > tooth length

* Morphology of the teeth:
  > the number of cusps of molars
  > shape / form of teeth

*Characteristic symptoms*

The characteristic symptoms can be divided in dental, oral and extra-oral symptoms. Table 1.2 shows the definitions.

**Table 1.2** *Definition of characteristic symptoms.*

* Dental symptoms
  > abnormalities in number, size and form of teeth etc.;
  i.e. anomalies of teeth

* Oral symptoms
  > abnormalities of lips, frenulae, tongue, palate etc.;
  i.e. anomalies in and around the mouth (teeth excepted)

* Extra-oral symptoms:
  > abnormalities of the skin, hair, nails, limbs etc.

*Oligodontia isolated and as part of a syndrome*

The following criteria were used to distinguish between the different groups; only the patients who were diagnosed by a medical specialist (paediatrician; clinical geneticist) or other specialist as oligodontia/S, were classified as such. When any doubt existed as to whether a patient had oligodontia/I or oligodontia/S, the patient was classified as oligodontia/I-S. All other patients with six or more congenitally missing teeth, excluding the third molars, were classified as patients with oligodontia/I.

*Abbreviations*

The abbreviations used to denote the teeth are given in table 1.3.

**Table 1.3** *Abbreviations used to denote the teeth.*

| | | | | Maxilla | | Mandible | |
|---|---|---|---|---|---|---|---|
| | | | | Right | Left | Left | Right |
| Central incisor | = | I1 | = | 11, | 21 | 31, | 41 |
| Lateral incisor | = | I2 | = | 12, | 22 | 32, | 42 |
| Canine | = | C | = | 13, | 23 | 33, | 43 |
| First premolar | = | P1 | = | 14, | 24 | 34, | 44 |
| Second premolar | = | P2 | = | 15, | 25 | 35, | 45 |
| First molar | = | M1 | = | 16, | 26 | 36, | 46 |
| Second molar | = | M2 | = | 17, | 27 | 37, | 47 |

This thesis is organized as follows: in Chapter 2, a review of the literature concerning the definition, prevalence, symptoms and etiology of oligodontia is presented.

In Chapter 3 a brief introduction is given of the different groups of patients with oligodontia and control groups that participated in the study. In addition, instruments used and procedure followed are described.

The prevalence and the distribution of congenitally missing teeth in the Netherlands are presented in Chapter 4.

In Chapter 5, a description is given of the measurements on dental casts. The mesiodistal dimensions of the teeth were measured and compared with a control group. Evaluated were the changes in tooth morphology.

In Chapter 6, the radiological findings, i.e. dental age, taurodontism and length of teeth, are presented. The results, once again were compared with a control group.

In Chapter 7, oral and extra-oral symptoms occurring in patients with oligodontia are described. Comparisons were made between patients with oligodontia/I and oligodontia/S and between patients with oligodontia/I and a control group. Additionally, associations between combinations of extra-oral symptoms and congenitally missing teeth were studied.

Possible environmental factors and pedigree analyses of families with oligodontia and are outlined in Chapter 8.

In Chapter 9, a comparison is made between patients with oligodontia and patients with syndromes, such as Down syndrome and 45,X/46,XX females. A contribution is made to the etiology of oligodontia.

Finally, the results are discussed in Chapter 10. Clinical consequences and recommendations for further research are given in this Chapter as well.

# Chapter 2
# Review of literature

## 2.1 Introduction

In this Chapter, a review will be given of the literature regarding the definition and prevalence of oligodontia, various symptoms and etiological factors.

## 2.2 Oligodontia: definition and prevalence

*Definition*

In literature, there is no consensus at all concerning the terminology used to describe a reduction in number of teeth. Many different terms are used to describe congenitally missing teeth. Most of the terms used in literature are listed in Table 2.1 (Jorgenson, 1989). The terms most frequently used are hypodontia, oligodontia and congenitally missing teeth (Haavikko, 1971; Buenviaje and Rapp, 1984; Bazan, 1985).

Oligodontia is derived from the greek root "oligos" which means few. The question is whether few teeth are missing or few teeth are present (Jorgenson, 1989). What is meant if the term oligodontia is used in literature?

**Table 2.1** *Terms used to describe the congenital missing of teeth.*

| | |
|---|---|
| Hypodontia | Agenesis |
| Congenitally missing teeth | Absence of teeth |
| Oligodontia | Deficient dentition |
| Anodontia | Dental anomaly |
| Severe hypodontia | Lack of teeth |
| Pseudoanodontia | Partial anodontia |

In literature, oligodontia is mostly defined as the congenital missing of a large number of teeth (Steen, 1986; Jorgenson, 1989; Lai and Seow, 1989). The question is: what can be defined as a large number? No consensus can be found concerning this question. Some define oligodontia as the missing of one or more teeth (Ruprecht et al., 1986). Stewart et al. (1982) and Hall (1983) reported that there are only two terms which clearly describe the absence of teeth: oligodontia, which is the absence of a number of teeth and anodontia which is the total absence of teeth.

Often the term hypodontia is used to denote the congenital missing of teeth. Hypodontia is often described as the missing of one or more teeth (Hunstadbraten, 1973; Winstanley, 1984; Bazan, 1985; Nik-Hussein and Salcedo, 1987). Silverman and Ackerman (1979) defined hypodontia as the absence of two or more teeth. Lai and Seow (1989) described hypodontia as the absence of one or a few teeth. Rune and Särnas (1974) defined severe hypodontia as the congenital missing of four or more teeth. Whisth et al. (1974) and Hobkirk and Brook (1980) gave the following definition of severe hypodontia: the missing of six or more teeth, excluding the third molars. The

frequency of agenesis of third molars varies from 1.3 to 36.6% (Grahnen, 1956); therefore, third molars were often excluded when defining oligodontia.

*Prevalence*

There have been numerous surveys made to study the prevalence of congenitally missing teeth. In Table 2.2, a listing is given. In those studies the third molars were not taken into account.

One of the earliest surveys was conducted by Dolder in 1936. Out of 10,000 Swiss schoolchildren, ranging in age from six to fifteen years, 3.4% were reported to have congenitally missing teeth. In 0.7%, more than two teeth were missing (Dolder, 1937).

Werther and Rothenberg (1939) reported that, of 1,000 children who attended a dental school clinic, 2.3% had congenitally missing teeth. Only 0.3% were missing more than two teeth.

Hunstadbraten (1973) reported that 10.1% of 1,295 schoolchildren, who also attended a dental school clinic, had congenitally missing teeth. In this study 2.5% were missing more than two teeth.

As seen in Table 2.2, the other frequencies reported are within this range of 2.3% to 10.1%. Generally the groups consisted of schoolchildren between 3-18 years of age, as well as some adults, attending dental clinics.

Congenitally missing deciduous teeth is very rare; reported frequencies vary from 0.1% to 0.9% (Ooshima et al., 1988).

## 2.3 Symptoms

The dental and oral symptoms occurring in both isolated oligodontia and in oligodontia as part of a syndrome will be described.

### 2.3.1 Dental and oral symptoms

The main dental and oral symptoms are given in Table 2.3.

**Table 2.3** *Main dental and oral symptoms of oligodontia.*

| |
|---|
| Congenitally missing teeth |
| Reduction in size and form of teeth |
| Reduction in size and form of the alveolar process |
| Delayed eruption of teeth which are present |
| Anomalies of the enamel |
| Increased free-way space |
| Cleft lip/palate |
| Other associated dental and oral anomalies |

**Table 2.2** *Prevalence of oligodontia.*

| Name | Sample size | Age range | Frequency of oligodontia | Percent missing more than two teeth | Most commonly missing teeth | Male/female difference | Jaw dominance | Date of study |
|---|---|---|---|---|---|---|---|---|
| Dolder | 10,000 | 6-15 | 3.4 | 0.7 | P2i, P2s, I2s | None | Mandible | 1936 |
| Werther and Rothenberg | 1,000 | 3-15 | 2.3 | 0.3 | I2s, P2i, P2s | None | Maxilla | 1936 |
| Byrd | 2,835 | 4-14 | 2.8 | N.R. | P2i, I2s, P2s | Female | N.R. | 1943 |
| Grahnen | 1,006 | 11-14 | 6.1 | 0.9 | P2i, I2s, P2s | None | Mandible | 1956 |
| | 1,064 | 17-43 | 5.0 | 1.0 | P2i, I2s, P2s | None | Maxilla | 1956 |
| Brown | 5,276 | 6-15 | 5.0 | 1.0 | P2i, I2s, P2s | Female | N.R. | 1957 |
| Glenn | 777 | 3-16 | 5.15 | <0.6 | P2i, I2s, P2s | Female | Mandible | 1961 |
| | 925 | 3-15 | 5.08 | 0.6 | P2i, I2s, P2s | Female | Mandible | 1964 |
| Rose | 6,000 | 7-14 | 4.3 | 0.6 | P2i, I2s, P2s | Female | N.R. | 1966 |
| Blayney and Hill | 13,033 | 12-14 | 3.86 | 0.4 | P2i, P2s, I2s | Female | Maxilla | 1967 |
| Muller et al. | 14,940 | 11-15 | 3.49 | N.R. | I2s, P2i, P2s | Female | Maxilla | 1970 |
| Haavikko | 1,041 | 5-13 | 7.97 | 0.97 | P2i, P2s, I2s | Female | Maxilla | 1971 |
| Hunstadbraten | 1,295 | 7-14 | 10.1 | 2.5 | P2i, P2s, I2s | Female | Mandible | 1973 |
| Silverman and Ackerman | 4,032 | 3-18 | 4.34 | 0.85 | P2i, I2s, P2s | N.R. | Maxilla | 1979 |
| Ruprecht et al. | 1,581 | 0-69 | 5.0 | 0.9 | I2s, P2s, I1i | N.R. | Maxilla | 1986 |

**Legend Table 2.2:**
I2s = lateral maxillary incisor
I1i = central mandibular incisor
P2s = second maxillary premolar
P2i = second mandibular premolar
N.R. = Not Reported

*Congenitally missing teeth*

The diagnosis of congenitally missing teeth usually was based on radiographic absence. The history of extraction or exfoliation must be negative (Bazan, 1985).

Teeth most frequently missing were second upper and lower premolar, upper lateral incisor and lower central incisor (Whisth et al., 1974; Lai and Seow, 1989). However, the order in which those four teeth normally appear was different in the various publications (Table 2.2).

Muller et al. (1970) described a symmetrical distribution of the missing teeth. Graber (1978) also found a symmetrical distribution over the left and right sides. In literature, a consensus as to whether teeth were more frequently missing in the maxilla or mandible does not exist (Table 2.2). Some authors reported a greater incidence of maxillary missing teeth (Muller et al., 1970), whereas others observed a greater incidence of mandibular missing teeth (Hunstadbraten, 1973). Rune and Särnas (1974) reported that there was no difference in sex ratio. In contrast, Whisth et al. (1974) reported a female preponderance. There are a few reports of hypodontia in the deciduous dentition with permanent successors (Ooshima et al.,1988).

*Reduction in size and form of teeth*

Reduced form of teeth is the second characteristic described (Fig. 2.1). Conical or peg-shaped incisors were observed (Warnakulasriya, 1989). Other authors reported a reduction in number of cusps of lower molars (Lavelle et al., (1970). Well described is the association of reduction in tooth size with oligodontia. Several authors described a reduction in mesiodistal dimension of the teeth as compared to a control group (Garn and Lewis, 1970; Baum and Cohen, 1971; Rune and Särnas, 1974; Brook, 1984). So far, no studies have been performed to measure the labiolingual dimension of the teeth in patients with oligodontia. Oliver et al. (1975) and Schuurs (1988) described cases in which a correlation had been made between oligodontia and short roots. Roberts (1973) also noted shortened second premolar roots in family members of families with a history of congenitally missing second premolars.

*Reduction in size and form of the alveolar process*

Absence of teeth results in an underdevelopment of the alveolar process (Fig. 2.2; Roeters, 1982; Schuurs, 1988). Particularly patients with ectodermal dysplasia often show an underdevelopment of the alveolar process, due to the large number of missing teeth (Oliver et al., 1975; Hobkirk and Brook, 1980; Bergendal et al., 1991).

*Delayed eruption*

No consensus exists in literature on the subject of delayed eruption. Some authors described a significant delay of eruption (Rune and Särnas, 1974; Ranta, 1986), whereas others reported that this was not the case (Bailit et al., 1968). Ranta (1984a,b) described a delayed eruption of teeth in patients with a cleft palate and hypodontia. The eruption was more severely delayed when a large number of teeth was missing (Ranta, 1984a,b).

*Anomalies of the enamel*

Anomalies of the enamel are described mostly in patients with oligodontia as part of a syndrome, for example the Ectrodactyly - Ectodermal dysplasia - Clefting (EEC) syndrome (Schuurs, 1988). Other syndromes in which both oligodontia and enamel

hypoplasia have been described were Down syndrome (Gorlin et al., 1990), Rieger syndrome (Drum et al., 1985), Rapp-Hodgkin syndrome (Crawford et al., 1989) and Ellis-Van Creveld syndrome (Himmelhoch and Mostofi, 1988).

*Increased free-way space*

Due to the congenitally missing teeth and a lack of alveolar growth an increased free-way space can be observed in patients with oligodontia. Facial appearance may mimic that of the edentulous person with mandibular protrusion and lip eversion (Fig. 2.3; Hobkirk and Brook, 1980).

**Figure 2.1** *Conical teeth in a patient with oligodontia.*

**Figure 2.2** *Underdevelopment of the alveolar process due to congenitally missing teeth.*

**Figure 2.3** *A patient with a deep set plica mentalis.*

**Figure 2.4** *Large diastemas in a patient due to multiple congenitally missing teeth.*

*Cleft lip/palate*

Clefting is described mostly in patients with oligodontia as part of a syndrome, EEC syndrome for example (Schuurs, 1988). Therefore, a more detailed description of clefting is given in paragraph 2.3.2. Ranta et al. (1983) described the association of hypodontia with cleft palate. The hypodontia was more severe with increasing extension

of the cleft. Hall (1983) reported the occurrence of oligodontia in 22 of the 55 clefting syndromes. Oligodontia was defined as the missing of a number of teeth.

*Other reported associated dental and oral anomalies*

Spyropoulos et al. (1979) described the simultaneous occurrence of hypodontia and hyperdontia. Nik-Hussein and Salcedo (1987) reported double teeth with hypodontia in identical twins. The right primary maxillary central incisor was fused with a supernumerary tooth and the left primary mandibular lateral incisor was missing. Roberts (1973) reported the association of ankylosis with oligodontia. Ruprecht et al. (1986) also described the occurrence of ankylosis, short roots and fusion in patients with hypodontia. According to them the findings could be incidental or associated. Lai and Seow (1989) also described the association of hypodontia with ankylosis of primary molars, taurodontism, enamel hypoplasia and peg-shaped incisors.

Järvinen (1984) reported a case with congenitally missing first permanent molars and ectopic eruption of the teeth present. Association of malposition of the cuspids and hypodontia was described by Svinhufvud et al. (1988).

In patients with Ellis-Van Creveld syndrome, serrating or notching of the alveolar ridge can be observed (Biggerstaff and Mazaheri, 1968). Also observed in these patients was a fusion of the middle portion of the upper lip to the maxillary gingival margin so that no mucobuccal fold or sulcus is present (Gorlin et al., 1990).

Finally, diastemas can be the result of a large number of missing teeth (Fig. 2.4).

### 2.3.2 Extra-oral symptoms associated with syndromes

Oligodontia is a finding which is reported as a symptom in more than one hundred syndromes (Appendix 1). All symptoms occurring with these syndromes can therefore occur in patients with oligodontia as part of a syndrome. The extra-oral and oral symptoms of the syndromes with which the dental practitioner will be confronted with most will be described here briefly. These syndromes are listed in Table 2.4.

**Table 2.4** *Syndromes in which oligodontia is an important feature.*

| |
|---|
| Ectodermal dysplasia (both hypohidrotic and hyperhidrotic) |
| Clefts (all types) |
| Rieger syndrome |
| Ellis-Van Creveld syndrome |
| Incontinentia pigmenti (Bloch-Sulzberger syndrome) |
| Ectrodactyly- Ectodermal dysplasia- Clefting (EEC) syndrome |
| Lacrimo-Auriculo-Dento-Digital (LADD) syndrome |
| Hair-nail-skin-teeth dysplasias |
| Tooth and nail syndrome |

*Ectodermal dysplasia*

This group of syndromes is heterogeneous, clinically as well as genetically. The patients are characterized by hypo- or hyperhidrosis, hypotrichosis and congenitally missing teeth. Incidence is about 1/100.000 births (Clarke, 1987). Minimal expression

of the syndrome with congenitally missing teeth and/or teeth with conical crown form and reduction in sweating and body hair in a patchy distribution may be observed in carrier females (Clarke, 1987). Nakata et al. (1980) described a reduced mesiodistal dimension of teeth in female carriers.

Frontal bossing, usually marked, and a depressed nasal bridge emphasize the small appearance of the face (Shapiro et al., 1984). Around the eyes, there are often fine linear wrinkles and pigmentation (Söderholm and Kaitila, 1985). Due to the absence of teeth and the resulting reduced vertical height, the lips are protuberant.

Cephalometric and anthropometric studies of hemizygotes and heterozygotes have shown a small lower facial height and depth, small palatal and cranial base widths, small malar bones, small calvarial height, prominent forehead, depressed nasal bridge and high-set orbits (Bixler et al., 1988).

Hypohidrosis is a characteristic symptom of one of the types of ectodermal dysplasia. Because other physical features of this syndrome are not so apparent in the first year of life, the child may present a "fever of unknown origin". An inability to sweat causes intolerance to heat, because eccrine sweat glands are severely reduced in number (Gorlin et al., 1990). The skin is soft and thin. Dryness of the skin, often severe, is due to the absence of sebaceous glands. Eczema is observed predominantly during the first years of life.

Hair of patients with ectodermal dysplasia show changes of distribution, structure, quality and amount. The body is usually devoid of lanugo hair. Scalp hair is often blond, fine, stiff and short (Fig. 2.5). Individual hairs are described as fine, brittle, dry and hypopigmented (Holbrook, 1988). Eyelashes and eyebrows are scanty or often absent.

Conditions in the nails of these patients range from incomplete formation to gross structural abnormalities to total nail absence (Fig. 2.6). Nails can be hyperconvex, conical, narrow or broad in shape. Nails can also be greatly thickened or formed as a thin atrophic membrane like structure (Holbrook, 1988).

Lacrimal gland function can be diminished or increased (Grant and Falls, 1944; Pinheiro and Freire-Maia, 1979). Ectodermal dysplasia sometimes has an X-linked recessive inheritance (Gorlin et al., 1990).

*Clefts (all types)*

The dental practitioner is probably most frequently confronted with clefting (Schuurs, 1988). Maxillary clefts of the primary and/or secondary palates are included among the more common congenital anomalies. Clinically, there is great variation in degree of cleft formation (Gorlin et al., 1990). A cleft may involve only the upper lip or may extend to involve the nostril and the hard- and soft palate. Combinations of cleft lip and palate are most common (Gorlin et al., 1990). The incidence of cleft lip with or without cleft palate shows a marked racial predilection. The frequency in white births in the USA ranges from 0.7 -1.3 (Gorlin et al., 1990).

*Rieger syndrome (hypodontia and primary mesodermal dysgenesis of the iris)*

The major features of Rieger syndrome are absent teeth, malformations of the anterior chamber of the eye and umbilical anomalies. The syndrome has an autosomal dominant inheritance with almost complete penetrance and variable expressivity (Drum et al., 1985). Characteristics of the facies include broad flat nasal root and prominent

supraorbital ridges. Also seen is relative prognathism due to underdevelopment of the maxilla and/or to loss of vertical height because of the congenitally missing teeth (Childers and Wright, 1986).

Abnormal development of the anterior chamber of the eye is characteristic of this syndrome. Pupils may be displaced (Gorlin et al., 1990). Other anomalies of the eye which can occur are microcornea, strabismus, glaucoma a.o. (Rogers, 1988). The periumbilical skin also fails to involute (Drum et al., 1985).

*Ellis-Van Creveld syndrome (chondroectodermal dysplasia)*

The most important features of this syndrome are bilateral postaxial polydactyly of the hands, chondrodysplasia of long bones resulting in acromesomelic dwarfism, ectodermal dysplasia affecting nails and teeth, and congenital heart malformations (Gorlin et al., 1990). The syndrome has an autosomal recessive inheritance pattern (Rosemberg et al., 1983).

Fusion of the middle portion of the upper lip to the maxillary gingival margin, with the result that no mucobuccal fold or sulcus is present anteriorly, is one of the most constant findings (Gorlin et al. 1990). Nearly all patients have severe dystrophy of the fingernails.

*Incontinentia pigmenti (Bloch-Sulzberger syndrome)*

Both X-linked and autosomal dominant types of inheritance have been suggested in this syndrome (Lucas, 1974; Sommer and Liu, 1984). Three clinical stages can be discriminated in skin lesions. The first stage is present at birth or starts just after birth. Linear or grouped vesicles can be noted on the extremities. At about one month of age, hyperkeratotic, warty lesions can be observed on the dorsal surface of the digits, knuckles, joints and limbs; this is the second stage. The third stage is characterized by brownish-grey maculas, starting between the third and sixth months of life. The pigmentation may begin to fade around the age of two years (O' Brien and Feingold, 1985). Alopecia of the atrophic, scarring type is seen near the apex of the crown of the head. Some of the anomalies of the eyes which are found in patients are strabismus, cataracts and optic atrophy (Francois, 1985).

In those patients, the central nervous system can also be involved (Gorlin et al., 1990). Paresis of eye muscles, microcephaly and mental retardation were associate findings described (Jones, 1966).

*Ectrodactyly-Ectodermal dysplasia-Clefting syndrome* (EEC)

This syndrome consists of lobster-claw anomalies of the hands and feet (Fig. 2.7), nasolacrimal duct obstruction, and cleft-lip palate (Gorlin et al., 1990). Anomalies of the eyes described are absent lacrimal punctae associated with dacryocystitis, keratoconjunctivitis, and photophobia (Leibowitz and Jenkins, 1984).

Hypopigmentation of skin and hair are sometimes present. Scalp hair, eyebrows and lashes are sparse. Nails are nearly always dystrophic. Kidney and ureter malformations are also described in some patients (Kaiser-Kupfer, 1973).

*LADD syndrome (Lacrimo-auriculo-dento-digital syndrome, Levy-Hollister syndrome)*

This condition is autosomal dominantly inherited. Hennekam (1987) suggested that the syndrome represents incomplete expression of the EEC syndrome. Most important

features of this syndrome are either recurrent, chronic, or absent tearing, recurrent or chronic conjunctivitis, absence or hypoplasia of lacrimal glands or punctae, canaliculae, tear sacs or nasal ducts. Pinnae can be cup-shaped, with or without hearing loss. Agenesis of salivary glands is also found. Limb and hand abnormalities reported were: fingerlike, bifid, or hypoplastic thumbs, syndactyly of second, third, and/or fourth digits and clinodactylous fifth digits (Wiedemann and Drescher, 1986).

**Figure 2.5** *A patient with ectodermal dysplasia with a different quality and amount of hair.*

**Figure 2.6** *Structural abnormalities of nails in a patient with ectodermal dysplasia.*

**Figure 2.7** *Lobster-claw anomalies of the hand of a patient with EEC syndrome.*

*Hair-nail-skin-teeth dysplasias*

Freire-Maia and Pinheiro (1984) described a large number of disorders involving dysplasia of hair, nails, skin and teeth. These dysplasias are of the same kind as those described under ectodermal dysplasia. Hair on body and scalp is often sparse. Nails are brittle and dystrophic. Skin is dry; hyperkeratosis can be observed, as can erythema and telangiectasia (Fadil et al., 1983).

Teeth show either enamel dysplasia, microdontia or hypodontia/ oligodontia.

*Witkop tooth-nail syndrome*

This syndrome is characterized by congenitally missing teeth and nail dystrophy. Autosomal dominant inheritance has been suggested for this syndrome (Gorlin et al., 1990). However, heterogeneity cannot be excluded (Hudson and Witkop, 1975). The findings in teeth and nails are the same as described before.

## 2.4 Etiology

Concerning the etiology of congenitally missing teeth both genetic and environmental factors are important. Missing teeth can be either a congenital or acquired anomaly. The etiology of both congenital and acquired absence of teeth (environmental and genetic factors) will be described in this paragraph. A well known example of environmental factors is the use of certain drugs. The stage of development, along with the length of the disruption, are important factors influencing the expression of the anomaly as well as which teeth will be affected. Genetic variation can be found at each stage of dental development, from the initiation of a tooth germ to the functional attachment of the resulting fully formed tooth in the bone of the jaw (Sofaer, 1975).

### 2.4.1 Etiological factors

The evolution theory was one of the earliest explanations for congenitally missing teeth (Schultz, 1932). The theory described a new dentition formula. Instead of the 32 teeth human beings now have, the new dentition will consist of 20 teeth. This will include one incisor, one canine, one premolar and two molars in each quadrant. The size of the jaw will be smaller and unable to accommodate the original complement of teeth (Jorgenson, 1980; Meller and Waterman, 1978).

Werther and Rothenberg (1939) summarized the etiological factors of oligodontia as follows: (as cited by Grahnen, 1956); 1) local influences on the jaws, 2) constitutional diseases, 3) trophoneurotic and endocrine disturbances and 4) inheritance.

*Local causes*

Werther and Rothenberg (1939) listed local causes such as sequestrating osteomyelitis, osteitis, trauma of different kinds, fractures and surgical procedures. An example of a trauma was the extraction of a deciduous tooth with removal of the permanent tooth germ at the same time, resulting in a missing tooth. Roentgen and radium rays can inhibit the development of tissue, especially during the period of most active growth. Weyman (1968) described the occurrence of hypodontia in patients with tumours of the face who were irradiated at the age of 8 weeks to 3 years. Lee et al. (1989) described hypodontia in irradiated beagle dogs. Hypodontia was age-dependent and dose-related.

Axrup et al. (1966) reported congenitally missing teeth in children whose mother had used Thalidomide[R] during pregnancy.

Meller and Waterman (1978) stated that jaw growth is intimately related to tooth development, according to the concepts of Osborn (1973). As tooth buds were initiated they inhibited further growth around them until they were adequately spaced. When spacing was not adequate, fusion of two tooth germs could occur, influencing the number of teeth.

Welbury et al. (1984) described a higher incidence of hypodontia in children who had received chemotherapy at an early age. The occurrence of hypodontia could only partially be explained by the effects of the disease itself or chemotherapy. In another group of children who had a long-term remission from malignancy, failure in tooth development was recognised as a result of chemotherapy (Maguire and Craft, 1987).

The etiology of an abnormal number of teeth must lie in an early stage of tooth initiation or shortly after tooth initiation. One of the important controlling factors of tooth development is formed by neural crest cells. Deficits in these cells may result in a generalized loss of teeth owing to a lack of stimulation to the oral ectoderm (Meller and Waterman, 1978).

Jorgenson (1980) reported that agenesis of teeth was caused by a physical disruption of the dental lamina, which resulted in obliteration of the tooth buds. Such disruption was seen in disorders such as orofaciodigital syndrome and Ellis-Van Creveld syndrome. Stewart and Poole (1982) also pointed to physical obstruction or disruption of the dental lamina as a possible explanation.

*Constitutional diseases*

The constitutional diseases that cause hypodontia as described by Werther and Rothenberg (1939) are rickets, tuberculosis, parotitis and exanthematous fevers. Gregg (1941) and Evans (1947) described mothers infected with rubella during pregnancy and who gave birth to children with hypodontia. Congenital lues is also known to cause hypodontia in children. No definite etiologic relationship has been found between hypodontia/ oligodontia and constitutional diseases. However, it is known that diseases such as rickets can cause anomalies of enamel and dentin. Therefore, it is logical to assume that severe toxic damage may cause tooth germ destruction (Grahnen, 1956).

*Endocrine disturbances*

There were no studies suggesting that any particular endocrine disturbance could cause hypodontia. It has been shown, however that these disturbances can interfere with jaw development, eruption and mineralization of teeth, resulting in absence of teeth. A possible explanation of missing teeth is a metabolic imbalance of such a nature that a crucial metabolite for odontogenesis is absent.

In two groups of patients with hypopituitarism, the effect of the human growth hormone was investigated by Sarnat et al. (1988). The first group consisted of patients with isolated growth hormone deficiency. The second group consisted of patients with high immunoreactive growth hormone and IGF-I deficiency (Laron type of dwarfism, LTD). Patients with LTD, who could not benefit from the treatment with human growth hormone were missing third molars in 90% of the cases. Hypodontia with regard to other teeth was found in 30% of both groups.

*Genetics*

Animal experiments and studies of twins have shown that hypodontia in the vast majority of cases is genetically determined (Werther and Rothenberg, 1939). The heritable nature of abnormal tooth number was evident in monozygotic twins, indicating that the condition of missing teeth is an extreme expression of diminution in tooth size. A variation of expression of the genes responsible has been observed in twins (Gravely and Johnson, 1971). Heredity is one of the most important etiological factors of

congenitally missing teeth given in literature. The criteria for a genetic trait given by Jorgenson (1980,1983) are as follows: 1) in many patients there is no apparent environmental etiology, 2) a repetitive pattern has been shown in affected individuals, 3) hypodontia/oligodontia is more common among related than non-related individuals, 4) frequency differences among races have been shown and 5) differences in concordance among twins of differing zygosity have been shown.

It has been established that oligodontia (hypodontia) fulfils the criteria for a genetic trait (Jorgenson, 1983). Although it has been established that oligodontia (hypodontia), in the majority of cases, is the result of genetic factors, the mode of inheritance is still unclear. Many authors considered oligodontia (hypodontia) to be the result of a single gene. They suggested a mendelian pattern of inheritance. An autosomal dominant trait with incomplete penetrance and variable expressivity has often been offered as an explanation. Grahnen (1956) also suggested a dominant mode of inheritance, which was confirmed by Philip and Caurdy (1985) and Ranta (1985). However, Rosenberg Gertzman (1982) reported a pedigree with a probable X-linked transmission. The pedigree could be consistent with both X-linked dominant and recessive. All statements made by these authors were based on family studies.

Other authors considered oligodontia (hypodontia) to be a multifactorial trait. A polygenic model - the anomaly is the result of a number of genetic factors - was suggested by Suarez and Spence (1974), Chosack et al. (1975), Bailit (1975) and Brook (1984). Usually, a polygenic mode of inheritance is observed in continuous traits such as stature and intelligence (Chosack et al., 1975). However, some discontinuous traits such as cleft lip and palate also show a polygenic mode of inheritance (Carter, 1969). Absence of teeth is also a discontinuous variable. Chosack et al. (1975) assumed that hypodontia was the result of a polygenic inheritance with a threshold effect. Those individuals below the biological threshold for the genetic predisposition were unaffected, while those beyond the threshold were found to be affected. Bailit (1975) assumed that hypodontia is a quasi-continuous trait. Absence of teeth tends to occur around the extremes of a continuous variable such as tooth size. Figure 2.8 shows that a certain physiological threshold exists around which the presence of teeth changes into the absence of teeth. Brook (1984) proposes a similar model combining polygenic and environmental factors.

**Figure 2.8** *A genetic model for congenitally missing teeth. An example of a quasi-continuous trait.*

## 2.5 Discussion

*Definition*

There is clearly no consensus in literature concerning the definition of oligodontia. Authors use different terms and numbers of missing teeth in their definitions. A confusion of tongues is obvious. In the definitions of oligodontia, no attention has been paid so far to reduced form or size of teeth. However, as reported in many publications, reduction in tooth size is closely associated with oligodontia (Baum and Cohen, 1971; Brook, 1984). In fact, oligodontia is probably the most extreme form of reduction in tooth size. It could be important to pay attention to this association in defining oligodontia. It can be concluded that, so far, no precise definition of oligodontia has been given in literature.

*Prevalence*

The reported prevalence of congenitally missing teeth varied enormously. Several factors may be responsible for the differences reported in the frequency of this disorder. The frequency of congenitally missing of teeth may have changed with time. Table 2.2 shows an increase in frequency from Dolder (1937) with 3.4% to Hunstadbraten (1973) with 10.1%. However, in later studies the frequency decreases again to 5.0% (Ruprecht et al., 1986). The mean of the reported frequencies was 4.9%. In the surveys a mean frequency of 0.85% of patients with more than two congenitally missing teeth was found.

Different criteria or different techniques could have been used in assessing congenitally missing teeth. In Dolder's study (1937) for example in only doubtful cases radiographs were made, whereas Hunstadbraten (1973) had an orthopantomogram of every patient. Furthermore, ethnic and racial factors, sample composition and differences in distribution by sex and age could explain differences in frequency.

The teeth most frequently missing were upper lateral incisor and second upper and lower premolar. Disagreement is found concerning which jaw had the most missing teeth. Some surveys reported the maxilla as having the most missing teeth (Werther and Rothenberg, 1939; Muller et al., 1970) and others in the mandible (Glenn, 1961; Hunstadbraten, 1973)

*Symptoms*

The occurrence of extra-oral symptoms in patients with oligodontia/S are well documented in literature (Gorlin et al., 1990). However, for a dental practitioner, it is impossible to have insight into the symptoms of all entities where oligodontia makes up one of the features. In literature, correlations are described between patterns of missing teeth and extra-oral symptoms (Jorgenson, 1980). These patterns can also be helpful in diagnosing the patient. Moreover, existing correlations can give an indication concerning the etiology of the anomaly.

Some of the dental symptoms, however, are still open to discussion. Delayed eruption and reduced length of teeth are two oral symptoms in which controversial findings are reported. Some authors reported a significant delayed eruption (Rune and Särnas, 1974; Ranta, 1986), whereas others reported no significant delay in eruption (Bailit et al., 1968).

Reduced length was mentioned in case reports (Oliver et al., 1975), but no studies have been done in a population of patients with oligodontia. As described in Chapter 1, eruption and size of teeth are of importance when considering dental therapy. The reduction of the mesiodistal dimension of teeth is well documented in literature. However, a reduction in tooth form has been described only occasionally (Lavelle et al., 1970). To the author's knowledge, no data of labiolingual dimensions have been reported of patients with oligodontia. In Dutch patients with oligodontia, no research has been done so far concerning dental, oral and extra-oral symptoms.

*Etiology*

The exact etiology and pathogenesis of congenitally missing teeth is still unknown. Nowadays, it is generally agreed that there is an important genetic component to congenitally missing teeth. No consensus however, consists concerning the mode of inheritance. Oligodontia (hypodontia) is thought to be the result of a single gene (Grahnen, 1956; Philip and Caurdy, 1985) or caused by a multifactorial trait (Bailit, 1975; Brook, 1984). Brook (1984) recommended further examination of the proposed model, including family studies and more detailed measurements of tooth dimensions.

However, environmental factors may play a substantial role. In literature, several environmental factors such as high fever and irradiation have been reported to cause oligodontia.

## 2.6 Conclusions

It can be concluded from the literature review that the questions posed, as described in Chapter 1, were relevant questions. The answers to these questions will hopefully contribute to the knowledge of oligodontia.

# Chapter 3
# Materials and methods

## 3.1 Introduction

In this Chapter, materials and methods used will be described briefly. In paragraph 3.2, a description of the participants of the different parts of the study is given. In paragraph 3.3, the instruments used to answer the questions as formulated in Chapter 1 will be presented. Two main questionnaires were designed in order to get the necessary information. The questionnaires were: a clinical history and a family history. In addition, a protocol was developed for documentation of the symptoms occurring in patients. The procedure followed in examining patients is described in paragraph 3.4.

## 3.2 Selection and description of participants

### 3.2.1 Selection of participants

The only criterion used for selecting patients with oligodontia was the congenital missing of six or more teeth excluding the third molars. This missing of teeth was radiographically confirmed. In general, the radiographic confirmation of congenitally missing teeth is possible in patients of four years or older. From that age on, all teeth, excluding third molars are perceptible on an orthopantomogram. Other criteria such as sex and social status were not included.

Patients included in the study came from Departments of Oral-Maxillofacial Surgery, Prosthodontics and Special Dental Care in various regions of the Netherlands.

In some syndromes, additional symptoms make it necessary to give special attention and treatment to the patients. Those patients are treated in other institutes, for example in an institution for severely mentally handicapped people. Dental practitioners, in general, will not be confronted with these patients. Therefore, those patients with syndromes with severe symptoms, were excluded from the study.

The patients treated in general practice were also excluded from the study as a result of the selection procedure. But because of multidisciplinary problems, dental practitioners usually refer patients with oligodontia to a Department of Oral-Maxillofacial Surgery, Prosthodontics and Special Dental Care. The patients who are treated in general practice, therefore, are assumed, for the larger part to be patients who are missing fewer than six teeth. We may assume that a representative group was derived with the selection procedure followed.

The most important criterion used to select the control groups was the confirmation that a full permanent dentition was (or had been) present. As far as possible, persons with family members with congenitally missing teeth were excluded. The groups were matched for sex, race and age.

### 3.2.2 Description of participants

In this study, data of a total number of 332 patients with oligodontia were collected. Since the data collected were not complete for all patients, the number of patients participating in the different parts of the study was always lower than 332 (Table 3.1).

One hundred sixty-seven patients with oligodontia were examined personally. Age ranged from 4 to 45 years. Clinical data, orthopantomograms and casts were gathered from those patients. The results are described in Chapters 4-9. Additional orthopantomograms of 165 patients with oligodontia were gathered. The age of these patients ranged from 5 to 14 years. These orthopantomograms, together with the number of orthopantomograms available from the first 167 patients, were used to asses the dental age of the patients with oligodontia (Chapter 6). In Table 3.1, the items scored are listed, together with the number of participants. A detailed description of the groups is given in the various Chapters.

The controls collected can be divided into five groups, C1 to C5. For comparing the mesiodistal dimensions of the teeth, a control group (C1) was derived from data of normal individuals as reported by Moyers et al. (1976). A description of C1 can be found in Chapter 5.

For comparing dental age subjects of the Nijmegen Growth Study were used as a control group (C2). Dental age can only be rated before tooth formation is completed, unlike tooth length and taurodontism which can only be measured when tooth formation is completed. Therefore, in addition to the group C2, orthopantomograms of another group of normal individuals (C3) was used to assess the occurrence of taurodontism and to measure the length of the teeth. A detailed description of both C2 and C3 is given in Chapter 6. Furthermore, data from one group (C4) were collected to define the symptoms occurring in healthy persons. A detailed description is given in Chapter 7. Finally, data from labiolingual dimensions of teeth in a control group of normal individuals (C5) as reported by Townsend (1983) were used in Chapter 9.

## 3.3 Instruments

The instruments as mentioned in paragraph 3.1 - clinical history, family history and documentation of symptoms - will be characterized in further detail.

### 3.3.1 Clinical history

Upon examining the patient a specifically designed form was used. Main items were: (1) personal data, (2) health of mother and child during pregnancy and shortly afterwards, (3) family history, (4) physical appearance and (5) dentition and oral status.

Questions concerning the health of mother and child were asked to detect possible environmental factors, as will be described in Chapter 8. The mother was specifically asked about traumas, drugs and illnesses during or shortly before pregnancy. Furthermore, questions were asked concerning illnesses, traumas and other occurrences during the first three years of the patient's life.

Questions about family history were asked to determine whether the anomaly was familial or sporadic, in order to get a first impression about the possible genetic aspects of oligodontia.

Finally, physical appearance, dentition and oral aspects were evaluated in order to be able to describe the symptomatology of the patients.

The data from items (1) to (3) were obtained by questioning the adult patient or the accompanying parent of the infant patient. The data from items (4) and (5) were obtained by examining and questioning the patient.

**Table 3.1** *Distribution of the participants in the study.*

| Patients with oligodontia (N=332) | | Control groups C1-5 |
|---|---|---|
| **Chapter 4** | | |
| - Distribution of missing teeth (N=196) | | |
| **Chapter 5** | | |
| - Mesiodistal dimensions of the teeth (N=82) | ---> | Group C1 (N=410) (Moyers et al.; 1976) |
| **Chapter 6** | | |
| - Dental age (N=216) | ---> | Group C2 (N=3156) (Prahl-Andersen et al.; 1979) |
| - Length of teeth (N=117) and taurodontism (N=90) | ---> | Group C3 (N=91) |
| **Chapter 7** | | |
| - Inventory of symptoms (N=167) | ---> | Group C4 (N=135) |
| **Chapter 8** | | |
| - Pedigree analysis (N=50) | | |
| - Etiology (N=166) | | |
| **Chapter 9** | | |
| - Labiolingual dimensions of teeth (N=82) | ---> | Group C5 (N=265) Townsend (1983) |

*External examination*

The following items were examined for abnormalities: skin, hair, nails, sweat secretion, tear secretion, eyebrows, ears, nose and forehead.

The condition of the skin was judged by the examiner as well as by asking the patient whether there were any particular problems. The skin was noted as being dry only if there were problems reported throughout the year. Patients who had a dry skin only during summer were noted as normal.

Hair and eyebrows were judged by the examiner as well. Data recorded concerned whether hair and eyebrows were normal, sparse, absent or whether the patient had more hair or eyebrow growth than normal.

Fingernails and toenails were inspected. Attention was paid to the shape and strength of the nails. The patient was asked if the nails were brittle.

A history of excessive or diminished sweating and tearing was not quantitated. The patients was asked to report specifically when diminished or excessive sweating or tearing occurred. Sweating on hot summer days was not recorded as an increased sweat secretion.

The shape of the ears and the position on the head were recorded. Ears were examined when the patient was sitting erect in the dentist's chair. A horizontal plane was created by drawing an imaginary line parallel to the occlusal plane through the outer corners of the orbit. Ears were classified as low-set when the upper part of the ear was situated below the horizontal plane.

The shape of the nose can be very diverse. The following categories were used: a saddle nose, a broad nose and "normal" shape of the nose. No measurements were performed.

The patients was only considered to have frontal bossing if there was a clear prominence of the anterior portion of the frontal skull bone.

Scoring and classification of all the dysmorphic features was done from slides by an experienced clinical geneticist.

*Oral examination*

The following items were quantitated: (1) number of congenitally missing teeth and (2) tooth morphology. These items will be discussed in further detail in Chapters 4 and 5. Furthermore, the following items were evaluated: enamel, interocclusal distance, interrelationship of maxilla and mandible, tongue, lips and frenulae labialis, clefts and craniomandibular dysfunction.

Abnormalities of the enamel could only be determined if teeth had not been restored with crowns or other large restorations. Abnormalities included congenital and acquired defects such as amelogenesis imperfecta and abnormalities due to tetracyclines.

The patient was asked to sit erect for examination of the interocclusal distance. A point on the chin and on the nose were marked. The patient was asked then to swallow several times. The distance between the two points was then measured. The patient was then asked to achieve maximal occlusion, again the distance was measured. If the difference between the two measurements was less than 4 mm, the interocclusal distance was scored as being normal, otherwise it was considered to be abnormal.

The interrelationship of maxilla and mandible was evaluated when looking at the patient in profile. Profile was scored as either normal or abnormal. "Abnormal" meant that either the maxilla or mandible was retro- or prognathic.

The size and appearance of the tongue were examined. The size of the tongue was described as being large if the tongue was protruding and overlapping the teeth.

Also examined was the attachment of the frenulae labialis: was it normal or was there an attachment to the alveolar process.

Furthermore, the presence or absence of clefts, and the area in which the cleft occurred were noted.

Finally, the patient was asked whether he or she had any difficulties with chewing, yawning or other jaw movements. The patient was also asked if he/she experienced periods of pain or had a reduced capability to open the mouth.

### 3.3.2 Family history

A questionnaire was given to the patient or, in case of a minor, to the accompanying parent following examination. The questionnaire used to take the family history by the Clinical Genetics Centre Utrecht served as a model. Changes made in the questionnaire were directed to oligodontia. Specific questions pointing to symptoms of ectodermal dysplasia such as abnormalities of the nails, hair and sweat production were added.

Other items known to have no relationship with oligodontia, such as leukaemia or other forms of cancer, were left out.

To gain further insight into the mode of inheritance of oligodontia in a particular family, the family dentist was asked to furnish additional data on family members. Permission was obtained prior to requesting this information. These dentists were asked to fill in the status praesens and to make impressions of the dentition of the patients.

With the data from the questionnaire and those from the dentist, a pedigree was drawn.

### 3.3.3 Documentation of symptoms occurring in patients

In addition to the questionnaires described above, additional information was obtained such as casts of the dentition, slides of the facies and radiographs. As far as possible, all documentation was made according to a standard procedure. Radiographs were necessary to define the number of missing teeth and to determine which teeth were missing. However, only radiographs that had already been made were used. No new radiographs were made.

Casts of the dentition were made to perform the measurements. The impressions were made with a slow setting alginate. The models were poured with a hard plaster, which was treated following the prescriptions of the manufacturer.

## 3.4 Protocol

### 3.4.1 The procedure

The protocol was approved by the scientific commission of research on human beings at the Academic Hospital in Utrecht. Names and addresses of possible participants were obtained from the respective centres where they were treated. Patients received a letter with the request to cooperate in the study. Every centre composed its own letter, according to its individual wishes. The participants were always free to participate or to refrain. The examination did not interfere with their treatment.

*Clinical examination*

First the patient was informed personally about the study. Then, the clinical examination was performed (Paragraph 3.3.1). Documentation was obtained as described in paragraph 3.3.3. Finally, the family history questionnaire was handed over to the patient. Special attention was given to the anomalies asked for in this questionnaire to avoid misunderstanding.

# Chapter 4
# Prevalence and distribution of congenitally missing teeth in the Netherlands[1]

## 4.1 Introduction

Oligodontia, or the congenital missing of teeth, has been the subject of many studies in several countries. In most studies, the frequency of the congenital missing of one or more teeth was studied, as was described in Chapter 2 (Table 2.1). The reported prevalences vary from 2.3 to 10.1%.

Only a few studies reported the prevalence of the congenital missing of six or more teeth. The prevalence in this category varied from 0.05 to 0.31% (Table 4.1).

The distribution of the congenitally missing teeth is often studied together with the prevalence of the disorder. As reported in Table 2.1, some studies show a female preponderance, whereas in other studies no difference in the distribution of congenitally missing teeth was found between males and females. The same holds true for differences in distribution of congenitally missing teeth between the mandible and maxilla.

As described in Chapter 1 and 2, patients with oligodontia can be classified as isolated oligodontia (oligodontia/I) or as oligodontia as part of a syndrome (oligodontia/S). For genetic counselling, it is important to distinguish between oligodontia/I and oligodontia/S. In some studies, patients with other anomalies associated with oligodontia (patients with oligodontia/S) were excluded from participation in the study (Rune and Särnas, 1974). There were also studies which did not mention whether the patients studied showed any other abnormalities (Whisth et al., 1974; Silverman and Ackerman, 1979).

To the author's knowledge, there have been no studies in the Netherlands in which the prevalence or distribution of congenitally missing teeth were evaluated. Nothing is known, therefore, about the prevalence and distribution of the congenital missing of six or more teeth, excluding the third molars. It might be expected, however, that the prevalence is somewhere within the range as reported in other countries (Table 2.1). The prevalence and distribution of congenitally missing teeth are of importance in relation to the planning of dental services.

The aim of the present study was i) to give a rough indication of the prevalence of oligodontia in the Netherlands and ii) to examine the distribution of missing teeth, and determine possible differences between the patients with oligodontia/I and oligodontia/S.

## 4.2 Materials and methods

A questionnaire was developed for the dental practitioner in order to establish prevalence. Questions asked were: i) number of patients the practice comprised and ii)

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[1] Part of this chapter is an edited version of the manuscript entitled: "Distribution of missing teeth and tooth morphology in patients with oligodontia" (authors: van der Weide Y; Steen WHA; Bosman F), which has been published by the Journal of Dentistry for Children (59:133-140, 1992) and which is printed with permission of the publisher.

number of patients with oligodontia in the practice, and the age and sex of these patients. In order to be able to accurately judge the prevalence of oligodontia, the same questions were asked about patients with cleft lip with or without cleft palate. The prevalence in the Netherlands of cleft lip with or without cleft palate is known. Finally, the dental practitioners were asked to estimate the percentage of the total population of patients within the age ranges of 15-44 years.

**Table 4.1** *Prevalence of the congenital missing of six or more teeth as reported in literature.*

| Authors | Number of congenitally missing teeth | Frequency of occurrence | Sample composition |
|---|---|---|---|
| Haavikko (1971) | 6 | 0.2% (1:500) | Schoolchildren |
| Hunstadbraten (1974) | ≥ 6 | 0.31% (1:322) | Schoolchildren |
| Muller et al. (1970)<br>White persons<br>Black persons | ≥ 6 | 0.05% (1:1,922)<br>0.07% (1:1,481) | Students |
| Whist et al. (1974) | 6 | 0.12% (1:800) | Children who came in for routine orthodontic check |
| Silverman and Ackerman (1979) | ≥ 6 | 0.1% (1:1,000) | Orthodontic clinic |

Fifty dental practitioners throughout the entire country were sent a questionnaire; 37 questionnaires were returned. The data were assumed to be distributed according to a Poisson distribution. A mean percentage of occurrence and 95% confidence intervals were calculated.

The study of the distribution of congenitally missing teeth included 196 patients (100 males and 96 females) with oligodontia. According to the definition, the patients exhibited the congenital missing of six or more teeth, excluding the third molars. The mean age was 23 years, range 4 - 48 years. Patients were enlisted from nine Departments of Oral-Maxillofacial Surgery, Prosthodontics and Special Dental Care in various parts of the Netherlands. Of the 196 patients, 62 patients had oligodontia/S and 95 patients had oligodontia/I. In 39 patients, the diagnosis could not distinguish between oligodontia/I and oligodontia/S.

The following syndromes occurred in the patients with oligodontia/S: 56 patients had ectodermal dysplasia, in either the hypohidrotic or hyperhidrotic form; one patient had Rieger syndrome; two patients had EEC syndrome (Ectrodactyly- Ectodermal dysplasia-Clefting syndrome); two patients had Bloch-Sulzberger syndrome, also known as incontinentia pigmenti and one patient had Cutis marmorata teleangiectatica congenita.

Which teeth were congenitally missing in the 196 patients was scored using orthopantomograms. The distribution of missing teeth in males and females and over maxilla and mandible were studied. The differences in distribution on left and right sides was also studied. Discrimination between oligodontia/I and oligodontia/S allowed us to study possible differences in these groups. Chi-square tests and Student's t-tests were used to determine significant differences.

## 4.3 Results

### 4.3.1 Prevalence

The prevalence of the congenital missing of six or more teeth, excluding the third molars, in the Netherlands was 0.05% (1:2,000). For cleft lip with or without cleft palate a prevalence of 0.09% (1:1,111) was found. For patients with oligodontia, the 95% confidence interval was $0.04\% < \mu < 0.06\%$. For the patients with cleft lip with or without palate, the confidence interval was $0.07\% < \mu < 0.11\%$. On average, 60% of the patients in general practice were within the age range of 15-44 years. The prevalence in this population (15-44 years) was 0.08% (1:1,250) and 0.15% (1:667) for oligodontia and cleft lip and palate respectively.

### 4.3.2 Distribution of congenitally missing teeth

The results of the distribution of missing teeth are given in the Tables 4.2 - 4.4. The total population consisted of the two groups oligodontia/I (95) and oligodontia/S (62), and the 39 patients in which the diagnosis could not distinguish between oligodontia/I and oligodontia/S. Males were missing significantly more teeth than females (Table 4.2).

**Table 4.2** *Distribution of missing teeth: difference between oligodontia/I and oligodontia/S, males and females.*

| | Total group N = 196 | Oligodontia/I N = 95 | t-value | Oligodontia/S N = 62 |
|---|---|---|---|---|
| | Mean ± SD | Mean ± SD | | Mean ± SD |
| Males | 14.6 ± 6.0 | 13.2 ± 5.1 | t = 5.1 ** | 19.4 ± 5.6 |
| Females | 12.7 ± 5.2 | 11.7 ± 4.2 | t = 2.4 * | 14.7 ± 6.3 |
| | t = 2.4 * | t = 1.4 # | | t = 2.4 * |
| Total | 13.7 ± 5.7 | 12.6 ± 4.8 | t = 4.7 ** | 16.9 ± 6.4 |

**Legend Tables 4.2 - 4.4:**
* = P < 0.01; ** = P < 0.001; # = P > 0.01

**Table 4.3** *Distribution of missing teeth: maxilla and mandible.*

| | Total group N = 196 | Oligodontia/I N = 95 | Oligodontia/S N = 62 |
|---|---|---|---|
| | Mean ± SD | Mean ± SD | Mean ± SD |
| Maxilla | 6.7 ± 2.8 | 6.2 ± 2.3 | 8.8 ± 3.8 |
| Mandible | 7.0 ± 3.5 | 6.4 ± 3.1 | 8.1 ± 3.2 |
| | $X^2$ = 4.23 df = 1 # | t = 1.1 # | t = 1.1 # |

The difference in mean number of missing teeth between the groups oligodontia/I and oligodontia/S was significant: males with oligodontia/S were missing significantly more teeth than males with oligodontia/I. For females, the difference between oligodontia/S and oligodontia/I was also significant. Males with oligodontia/S were missing significantly more teeth than females with oligodontia/S. The difference between males with oligodontia/I and females with oligodontia/I was not significant (Table 4.2).

No significant differences were found in the distribution of missing teeth over maxilla and mandible and over the left and right side for males and females (Tables 4.3-4.4).

Figure 4.1 shows the percentages of missing teeth in maxilla and mandible. The second lower premolar was the tooth most frequently missing, followed by the second upper premolar, upper lateral incisor and lower central incisor.

**Table 4.4** *Total numbers of missing teeth on left and right sides of maxilla and mandible.*

| | Left | Right | $X^2$ df=1 |
|---|---|---|---|
| Oligodontia/I | 599 | 595 | 0.07 # |
| Oligodontia/S | 527 | 523 | 0.03 # |
| Total | 1345 | 1335 | 0.004 # |

**Figure 4.1.** *Distribution of the missing teeth in maxilla and mandible. The percentage missing of each tooth is shown.*

## 4.4 Discussion

The reported prevalences vary considerably in literature. The differences in frequency can be explained partly by racial factors and the sample composition of the various studies. Different criteria and different techniques used to assess the congenital missing of teeth can also lead to differences in frequency.

The age of the patients, for example, is important if one wants to establish the

presence or absence of teeth. When patients too young for determining clinically or radiographically the presence or absence of teeth are included in the study, an overestimation of the prevalence can result. When patients who are too old, for determining if teeth are congenitally missing or have been extracted are included in the study, an underestimation can result. From the age of four years on, all teeth are perceptible on an orthopantomogram, since calcification has begun. Only the third molars are still imperceptible from this age onwards. However, these were excluded from this study. From Table 2.1, it can be seen that some studies determined the prevalence of congenitally missing teeth in patients three years of age and older.

Another important criterion is the sample composition of the study. The composition of the population partly determines the level of prevalence. It can be expected that the prevalence of congenitally missing teeth in an orthodontic population is higher than in the general population, since patients with oligodontia often need orthodontic treatment.

Criteria such as age and sample composition only partly explain the differences in prevalence as reported in Table 2.1. The studies in which the patients of three years of age were included were not the studies with the highest prevalence. This was also true for the study of Rose (1966), where the prevalence of congenitally missing teeth was examined in an orthodontic population.

In the present study, a different method was used to reveal prevalence then the methods used in other studies. Dental practitioners were asked to report the prevalence in their practice. It was assumed that dental practitioners could remember patients with oligodontia, since they are still exceptional in general practice. It can be expected that using this method leads to an underestimation, since very young patients have not yet been diagnosed, and older patients have already been forgotten. The patients reported will be within the age range of 15 - 44 years. Therefore, the dental practitioner was asked to give an estimate of the number of patients in his practice who were within this range.

As noted in the materials and methods, the number of cleft lip with or without cleft palate patients served as a control for the oligodontia, since the prevalence of this anomaly in the Netherlands is known to be about 1:600 (Cornel et al., 1991). The frequency of cleft lip with or without cleft palate in the present study was found to be 1:1,111. The mean percentage of patients in the age range of 15-44 years was 60%. Calculating the frequency of patients with cleft lip with or without cleft palate in the age range of 15-44 years revealed a frequency of 1:667. This frequency is consistent with the frequency known 1:600. Therefore, it was assumed in the present study that the most reliable prevalence of oligodontia was the prevalence in the group of patients between the age of 15-44 years, which was found to be 1:1,250 or 0.08%. The frequencies of occurrence for oligodontia (0.05% and 0.08%) as found in the present study are within the range as reported by several authors (Table 4.1). Further, more extensive research is needed to determine more precisely the prevalence of oligodontia in the Netherlands.

The findings of the distribution of congenitally missing teeth presented are from patients with oligodontia who were treated in specialized dental centres. The findings do only represent patients missing six or more teeth, the third molars excluded.

Due to the selection procedure, patients treated in general practice were excluded from the study. If those patients had been included in the study, a reduction in the mean number of missing teeth might be expected, on the premise that the relatively simple

cases are treated in general practice.

Discrimination between oligodontia/I and oligodontia/S resulted in a significant difference in the mean number of missing teeth between males and females with oligodontia/S (Table 4.2). Literature shows that patients with ectodermal dysplasia are afflicted with a more severe form of oligodontia (Tiecke, 1965). Males with ectodermal dysplasia, often X-linked, show severer signs and suffer more afflictive symptoms than do females. This might explain the larger number of missing teeth in patients with oligodontia/S, particularly in the case of males with oligodontia/S, since the group consisted mainly of patients with ectodermal dysplasia.

Differences found between males with oligodontia/I and females with oligodontia/I were not significant. A significant difference in the distribution of missing teeth between males and females was found, however, when no discrimination was made between oligodontia/I and oligodontia/S. The difference found was one between males with oligodontia/S and females with oligodontia/S (Table 4.2). Whisth et al. (1974) report more missing teeth in females than in males. However, they do not discriminate between oligodontia/I and oligodontia/S. Rune and Särnas (1974) exclude patients with abnormal conditions other than missing teeth from their study and report no significant difference in the distribution between males and females; this is in agreement with our findings in the group with oligodontia/I.

No significant differences were observed in either oligodontia/I and oligodontia/S concerning distribution of maxillary and mandibular missing teeth; evaluations were made separately and by total population. However, a slightly greater number of teeth were found to be missing in the mandible. A consensus as to whether teeth are more frequently missing in the maxilla or mandible cannot be determined from literature. Some authors report a greater incidence of missing teeth in the maxilla (Muller et al., 1970) whereas others observe a greater incidence of missing teeth in the mandible (Whisth et al., 1974; Hunstadbraten, 1973).

No difference was observed, in the total population and in both groups evaluated separately, between the distribution of missing teeth over left and right sides when both maxillary and mandibular distributions were included. Such a symmetrical distribution is also found by Muller et al. (1970) and by Graber (1978). The second upper and lower premolar, upper lateral incisor and central lower incisor were most frequently missing (Fig. 4.1). Other investigations report the same result (Whisth et al., 1974; Lai and Seow, 1989). The most stable teeth were the upper central incisor and upper and lower first molars. These findings are in agreement with those as reported by Tso et al. (1985).

## 4.5 Conclusions

In the present study, a prevalence of oligodontia of 0.08% (1:1,250) was found. It is assumed that this is a reasonable indication of the true prevalence.

The distributions by left and right sides and by maxilla and mandible did not differ significantly. Apparently, both groups, oligodontia/I and oligodontia/S, differed only in the number of missing teeth. Therefore, it can be concluded that for a correct statement of patients with oligodontia, the two groups should be evaluated separately if the number of missing teeth is considered.

# Chapter 5
# Dental casts: Measurements and morphological changes of teeth[1]

## 5.1 Introduction

The morphology of teeth is influenced by genetic factors and environmental factors. The size of teeth of patients with oligodontia have been the subject of several studies, as was described in Chapter 2. Reduced mesiodistal dimensions of the teeth have been described by several authors (Baum and Cohen, 1971; Rune and Särnas, 1974). It is clear that reduction in tooth size is associated with oligodontia (Baum and Cohen, 1971; Rune and Särnas, 1974; Garn and Lewis, 1974; Brook, 1984). This reduction is sometimes seen, therefore, as a genetic expression of the same disorder, suggesting that oligodontia is not an isolated phenomenon (Cohen, 1971; Gravely and Johnson, 1971). The question is as to whether all teeth are equally affected or whether there is a gradient of reduction affecting some teeth more severely than others. The gradient of size reduction can be important in relation to pathogenesis.

Besides the reduction in size of teeth changes in tooth morphology are described in patients with oligodontia. In contrast with the mesiodistal dimensions only a few authors have described the changes in tooth morphology. Lavelle et al. (1970) described a correlation between reduction in tooth morphology of a lower molar and agenesis of the third molars. The variation in morphology consisted of a reduction in the number of cusps of lower molars. Davies (1968) also reported a cusp reduction in permanent mandibular first molars in patients with agenesis of teeth. The change in tooth morphology reported of most are conical or peg-shaped teeth (Warnakulasuriya, 1989).

The aim of the present study was to establish the gradient of reduction in tooth size and changes in tooth morphology.

## 5.2 Materials and methods

The study included 82 patients with oligodontia (41 males and 41 females). The mean age was 23 years, with age range being 11 to 42 years. A mean number of 13 congenitally missing teeth was found in these patients.

Patients were enlisted from nine Departments of Oral-Maxillofacial Surgery, Prosthodontics and Special Dental Care in various parts of the Netherlands.

Of the 82 patients 29 patients had oligodontia/S and 53 patients had oligodontia/I. The following syndromes occurred in patients with oligodontia/S: 28 patients had ectodermal dysplasia, in either hypohidrotic or hyperhidrotic form and one patient had Bloch-Sulzberger syndrome, also known as incontinentia pigmenti.

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[1] This chapter is an edited version of the manuscript entitled: "Distribution of missing teeth and tooth morphology in patients with oligodontia" (authors: van der Weide Y; Steen WHA; Bosman F), which has been published by the Journal of Dentistry for Children (59:133-140, 1992) and which is printed with permission of the publisher.

*Mesiodistal dimensions*

The mesiodistal dimensions were measured on casts, using a standard procedure. All impressions were taken with an alginate material, and poured in dental stone. Casts of 82 patients who had few or no dental restorations were collected.

The maximum mesiodistal dimension of a tooth was only measured if the tooth was fully erupted and no dental restorations were made. The measurements were made with a digital measuring instrument. The accuracy of this instrument was 0.01 mm. All measurements were recorded by one author (YSW).

Mesiodistal dimensions of left and right teeth were obtained, but in absence of statistically significant differences between the sides, values averaged from right and left measurements were used in the final analysis.

The mesiodistal dimensions of all teeth, except second and third molars, were made. The measurements were compared with standard mesiodistal dimensions recorded by Moyers et al. (1976).

*Tooth morphology*

For tooth morphology teeth were only given a score if they were without dental restorations. The scores were based on standards as recorded by Zeisz and Nuckols (1949).

The following scores were used: For incisors 1) normal, 2) slightly conical and 3) conical incisors (Fig. 5.1a). For canines 1) normal, 2) no cingulum and 3) conical canines (Fig. 5.1b). In case of premolars 1) normal 2) reduced palatinal/lingual cusp and 3) conical premolars (Fig. 5.1c). For molars 1) three-cusp type of occlusal pattern, 2) four-cusp type and 3) five-cusp type of occlusal pattern (Fig. 5.1d). Those classifications were used for both maxilla and mandible.

When it was not possible to define the right class in which the tooth belonged no score was given to that particular tooth.

*Statistical procedure and error analysis*

The statistical procedure for comparison of the mesiodistal dimensions of the teeth was as follows: first a Kolmogorov-Smirnov test was performed to confirm the normal distribution of the collected data, then an F-test was performed to test whether the standard deviations of both populations could be assumed equal. If the standard deviations could be assumed equal a Student's t-test for comparison of two means was used (Harnett, 1982). In the cases where the standard deviation could not be assumed equal, Welch's test for comparisons involving two variations that must be separately estimated was used (Pearson and Hartley, 1966).

Experimental errors were analyzed by a replicability trial in which the mesiodistal dimensions of the teeth, selected at random, were measured twice. Student's t-test was used to determine if there were significant differences between the first and second measurements. A mean difference of 0.042 mm was found for the mesiodistal measurements. The difference was not significant, neither was there evidence of systematic differences between the first and second measurements.

In evaluating the differences between the teeth concerning the changes in tooth morphology a test for comparison of two proportions were used (Armitage and Berry, 1987).

**Figure 5.1 (a-d)** *Standards used for scoring variation in tooth morphology based on standards given by Zeisz and Nuckols (1949).*

**Figure 5.1a** *Incisors, in this figure all upper incisors.*
*From left to right: 1) normal; 2) slightly conical; 3) conical.*

**Figure 5.1b** *Canines, in this figure all lower canines.*
*From left to right: 1) normal; 2) no cingulum; 3) conical.*

**Figure 5.1c** *Premolars, in this figure all upper premolars.*
*From left to right: 1) normal; 2) reduced palatinal cusp; 3) conical.*

**Figure 5.1d** *Molars, in this figure all upper molars.*
*From left to right: 1) three-cusp type of occlusal pattern; 2) four-cusp type; 3) five-cusp type.*

## 5.3 Results

### 5.3.1 Mesiodistal dimensions of the teeth

The mesiodistal dimensions of maxillary and mandibular teeth for males and females are given in the Tables 5.1 and 5.2.

In absence of significant differences between the mesiodistal dimensions of teeth of patients with oligodontia/I and oligodontia/S for both males and females, values of both groups were combined in the final analysis.

Almost all mesiodistal dimensions of maxillary and mandibulary teeth of females differed significantly from the mesiodistal dimensions of the teeth of the control group, with exception of the upper canine, upper second premolar and lower first molar (Table 5.1). The mesiodistal dimensions of upper central and lateral incisors and the first molars showed the greatest difference (D) of the mean. The greatest proportional differences (D%) were found with the lateral and central incisor.

**Table 5.1** *Mesiodistal dimensions of maxillary and mandibular teeth of females.*

| | N1 | X1 | SD | N2 | X2 | SD | p-value | D | D% |
|---|---|---|---|---|---|---|---|---|---|
| Maxilla | | | | | | | | | |
| I1 | 35 | 7.6 | 0.5 | 189 | 8.7 | 0.6 | < 0.001 | 1.1 | 13 |
| I2 | 11 | 6.0 | 0.5 | 172 | 6.8 | 0.6 | < 0.001 | 0.8 | 12 |
| C | 18 | 7.2 | 0.6 | 125 | 7.5 | 0.4 | N.S. | 0.3 | 4 |
| P1 | 13 | 6.2 | 0.6 | 122 | 6.6 | 0.5 | < 0.01 | 0.4 | 6 |
| P2 | 2 | 6.0 | 0.7 | 99 | 6.5 | 0.5 | N.S. | 0.5 | 8 |
| M1 | 34 | 9.5 | 0.8 | 192 | 10.2 | 0.6 | < 0.001 | 0.7 | 7 |
| Mandible | | | | | | | | | |
| I1 | 16 | 5.1 | 0.4 | 196 | 5.5 | 0.3 | < 0.01 | 0.4 | 7 |
| I2 | 25 | 5.3 | 0.4 | 189 | 5.9 | 0.3 | < 0.001 | 0.6 | 10 |
| C | 22 | 6.2 | 0.3 | 148 | 6.6 | 0.3 | < 0.001 | 0.4 | 6 |
| P1 | 28 | 6.4 | 0.4 | 134 | 6.8 | 0.7 | < 0.01 | 0.4 | 6 |
| P2 | 5 | 6.4 | 0.6 | 100 | 7.1 | 0.5 | < 0.01 | 0.7 | 10 |
| M1 | 30 | 10.3 | 0.7 | 191 | 10.3 | 0.7 | N.S. | 0 | 0 |

**Legend Tables 5.1 and 5.2:**
X1, X2 = mean mesiodistal dimension (in mm) of teeth of females
X3, X4 = mean mesiodistal dimension (in mm) of teeth of males
SD = standard deviation D = difference X1-X2 or X3-X4
N1,3 = sample size of patients with oligodontia N2,4 = N from Moyers et al. (1976)
D% = proportional difference of the mean (X1-X2)/X2 or (X3-X4)/X4

The mesiodistal dimensions of both maxillary and mandibular teeth of males were significantly reduced (Table 5.2). The mesiodistal dimensions of upper incisors, upper first molar and lower second premolar showed the greatest difference of the mean. The greatest proportional differences were found with the upper central and

lateral incisors and second premolars.

Figures 5.2 and 5.3 show that the mesiodistal dimension of the upper central incisor (Fig. 5.2) and upper first molar (Fig. 5.3) of females decrease, when the number of missing teeth increases. The correlation coefficients were significant ($P < 0.01$) for both teeth. A trend toward a similar correlation was observed for other teeth, although not as clearly significant as for those teeth.

### 5.3.2 Changes in tooth morphology

The results of the changes in tooth morphology are presented in the Tables 5.3 - 5.7. The incisors were in the majority of the cases normal (Table 5.3). The slightly conical incisor was the sort of variation seen mostly. The differences between the upper central and lower central incisor were significant ($P < 0.01$), as was the difference between upper central and lateral incisor.

Only a minority of the canines showed variation in morphology, mostly in the form of a conical canine. Of the lower canines 87% and of the upper canines 82% were normal, this difference between upper and lower canines was not significant ($P > 0.01$; Table 5.4).

**Table 5.2** *Mesiodistal dimensions of maxillary and mandibular teeth of males.*

| | N3 | X3 | SD | N4 | X4 | SD | p-value | D | D% |
|---|---|---|---|---|---|---|---|---|---|
| Maxilla | | | | | | | | | |
| I1 | 37 | 7.6 | 0.8 | 212 | 8.9 | 0.6 | < 0.01 | 1.3 | 15 |
| I2 | 6 | 5.6 | 0.4 | 201 | 6.9 | 0.6 | < 0.001 | 1.3 | 19 |
| C | 11 | 7.5 | 0.5 | 152 | 8.0 | 0.4 | < 0.001 | 0.5 | 6 |
| P1 | 13 | 6.1 | 0.6 | 157 | 6.8 | 0.5 | < 0.001 | 0.7 | 10 |
| P2 | 10 | 5.9 | 0.5 | 132 | 6.7 | 0.4 | < 0.001 | 0.8 | 12 |
| M1 | 32 | 9.6 | 0.9 | 216 | 10.6 | 0.6 | < 0.01 | 1.0 | 9 |
| Mandible | | | | | | | | | |
| I1 | 10 | 5.0 | 0.4 | 214 | 5.5 | 0.3 | < 0.001 | 0.5 | 9 |
| I2 | 16 | 5.5 | 0.4 | 208 | 6.0 | 0.4 | < 0.001 | 0.5 | 8 |
| C | 12 | 6.6 | 0.5 | 170 | 7.0 | 0.4 | < 0.01 | 0.4 | 6 |
| P1 | 27 | 6.5 | 0.5 | 159 | 6.9 | 0.6 | < 0.01 | 0.4 | 6 |
| P2 | 6 | 5.8 | 0.6 | 132 | 7.2 | 0.5 | < 0.001 | 1.4 | 19 |
| M1 | 31 | 10.3 | 0.7 | 215 | 10.7 | 0.6 | < 0.01 | 0.4 | 4 |

A reduced palatinal cusp was the sort of variation seen mostly in upper premolars (Table 5.5). The difference between second and first premolar was significant ($P < 0.05$), but with $P < 0.01$ the difference was not significant.

Of the lower premolars respectively 26 and 31% were normal, this difference between upper and lower premolars was not significant ($P > 0.01$; Table 5.6). A strongly reduced lingual cusp was the sort of variation seen mostly.

**Figure 5.2** *Mesiodistal dimension of the female maxillary central incisor, plotted against the number of missing teeth.*

*Correlation coefficient (R) = -0.63 (P<0.01); Point of intersection vertical axis = 8.7 (N=35)*

**Figure 5.3** *Mesiodistal dimension of the female maxillary first molar, plotted against the number of missing teeth.*

*Correlation coefficient (R) = -0.056 (P<0.01); Point of intersection vertical axis = 10.8 (N=34)*

**Table 5.3** *Changes in tooth morphology of the central and lateral incisors.*

| | I1 sup. | I2 sup. | I1 inf. | I2 inf. |
|---|---|---|---|---|
| Normal | 52 % | 34 % | 98 % | 98 % |
| Slightly conical | 43 % | 57 % | 2 % | 2 % |
| Conical | 5 % | 9 % | 0 % | 0 % |
| N | 143 | 35 | 53 | 82 |

z (I1 sup.-I1 inf.; normal) = 12.5 ($P < 0.001$)
z (I1 sup.-I2 sup.; abnormal) = 4.9 ($P < 0.01$)

**Legend Tables 5.3 - 5.7:**
inf. = inferior; sup. = superior.

Of the upper molars the sort of variation in occlusal pattern seen mostly was the three-cusp type. The difference between first and second molar was significant ($P < 0.05$). However, for $P < 0.01$ the difference was not significant. The lower molars showed in almost all cases the normal four and five-cusp type of occlusal pattern, the difference was not significant ($P > 0.01$; Table 5.7).

**Table 5.4** *Changes in tooth morphology of the canines.*

| | C sup. | C inf. |
|---|---|---|
| Normal | 82 % | 87 % |
| No cingulum | 0 % | 4 % |
| Conical | 18 % | 9 % |
| N | 66 | 71 |

z = 0.81 (P> 0.01)

**Table 5.5** *Changes in tooth morphology of the maxillary premolars.*

| | P1 sup. | P2 sup. |
|---|---|---|
| Normal | 34 % | 57 % |
| Reduced palatinal cusp | 56 % | 43 % |
| Conical | 10 % | 0 % |
| N | 59 | 35 |

z = 2.2 (P<0.05)

**Table 5.6** *Changes in tooth morphology of the mandibulary premolars.*

| | P1 inf. | P2 inf. |
|---|---|---|
| Normal | 26 % | 31 % |
| Reduced lingual cusp | 20 % | 37 % |
| Strongly reduced lingual cusp | 53 % | 26 % |
| Conical | 1 % | 6 % |
| N | 99 | 35 |

z = 0.56 (P> 0.01)

**Table 5.7** *Changes in tooth morphology of the maxillary and mandibulary molars.*

| | M1 sup. | M2 sup. | M1 inf. | M2 inf. |
|---|---|---|---|---|
| Three-cusp type | 41 % | 62 % | 1 % | 0 % |
| Four-cusp type | 48 % | 33 % | 22 % | 19 % |
| Five-cusp type | 11 % | 5 % | 77 % | 81 % |
| N | 126 | 39 | 76 | 16 |

z = 2.3 (P<0.05) (Three-cusp type M1 sup. - M2 sup.)
z = 0.26 (P>0.01) (Four-cusp type M1 inf. - M2 inf.)

## 5.4 Discussion

The findings presented are of patients with oligodontia treated in specialized dental centres. The findings do only represent patients missing six or more teeth, exclusive of the third molars.

Due to the selection procedure, patients treated in general practice were excluded from the study. Had those patients been included in the study, a reduction in the mean number of missing teeth might be expected, on the premise that the relatively simple cases are treated in general practice.

In the total population almost all mesiodistal dimensions were significantly reduced

compared with the mesiodistal dimensions of a normal population. These findings are in concordance with findings of other authors (Baum and Cohen, 1971; Rune and Särnas, 1974). In concordance with the findings of Brook (1984), males apparently showed greater differences of the mean than females (Tables 5.1 and 5.2).

Figures 5.2 and 5.3 show that the mesiodistal dimension, of the maxillary central incisor and first molar decrease when the number of missing teeth increases; indicating that in patients with multiple missing teeth, the crown-size reduction is severer. For those teeth in females, the correlation coefficients were significant. The other teeth showed more or less the same trend, not all correlation coefficients, however, were significant. It was striking, however, that for all teeth the points of intersection with the vertical axis had approximately the value of the mesiodistal dimension of the respective teeth of the control group. Garn and Lewis (1970) also reported an association between reduction in tooth number and crown-size reduction. As described in the previous Chapter, patients with oligodontia/S were missing significantly more teeth than patients with oligodontia/I. However, discrimination between oligodontia/I and oligodontia/S did not result in significant differences in mesiodistal dimensions of the teeth. Patients with oligodontia/S did not have smaller teeth than patients with oligodontia/I. This phenomenon can be explained by the mean number of missing teeth of the patients with oligodontia/S in this part of the study. The mean number of missing teeth in patients with oligodontia/I and oligodontia/S were very well comparable, namely a mean number of 12 and 15 congenitally missing teeth respectively.

A reduction in the number of cusps of both lower and upper molars is earlier reported by Kraus et al. (1970). Conical teeth are described by several authors in relation with oligodontia (Warnakulasuriya, 1989). In literature, no quantitative information could be found of variation in tooth morphology in normal populations. So no comparison could be made. No conclusions can be drawn whether there is more variation in the population of patients with oligodontia than there is in a normal population. Further research is needed to investigate this. The reduction in tooth morphology can be an important characteristic when confirming the mode of inheritance. Clinically, these reductions in morphology and size of teeth are of importance in relation with dental therapy.

Crowns of permanent teeth form throughout infancy and childhood (Moorrees et al., 1963), and their completed size is, in part, a reflection of the individuals morbidity, growth capacity, and general well-being (Bailit and Sung, 1968; Garn et al., 1979). As such, the dentition affords a means of assessing the growth "success" at various ages, stretching from infancy (when incisors and first molars are undergoing amelogenesis) to late childhood (when canines and premolars complete crown formation) (Werner and Harris, 1989).

If oligodontia was a localized, transient disruption in development, only teeth formed in the same period should be affected. In the Tables 5.1 and 5.2 it is shown that almost all teeth, both early and late-developing, were affected. Figure 4.1 also shows that both early and late-developing teeth (P2, I2) were frequently missing. However, in our study, not all teeth were equally affected. An interesting phenomenon was the greatest proportional difference of the central and lateral incisors and second premolars (Tables 5.1 and 5.2). Concordance can be seen with the teeth most frequently missing, namely lateral incisor and second premolar, as

shown in Figure 4.1. Bailit (1975) reported that not all teeth are equally heritable. The "key" tooth in each morphologic class has the highest heritability, and is the more stable tooth morphologically. The more distal tooth seem to be more influenced by the environment. As noticed, in our study the more distal teeth (P2, I2) seemed to be more severely affected. According to Bailit (1975) the severe reduction in mesiodistal dimension of lateral incisor and second premolar should, for the most part, be due to environmental factors. The development of the lateral incisor, however, takes place in the 5th/6th month of prenatal life, whereas the development of the second premolar starts in the 9th month postnatal. As such, it is more readily acceptable that those teeth were influenced by genetic factors. Another explanation could be the interaction of genetic and environmental factors, resulting in more severely reduced distal teeth.

## 5.5 Conclusions

It can be concluded from the present study, that the mesiodistal dimensions of almost all maxillary and mandibular teeth were significantly reduced compared to a control group. Changes in tooth morphology of all teeth were found.

The results, taking into account the relatively small number of measurements, support the hypothesis that oligodontia is not an isolated phenomenon, but is related to a complex of other dental changes.

# Chapter 6
# Tooth formation: Radiologic findings[1]

## 6.1 Introduction

Oligodontia is reported to be associated with dental abnormalities, such as reduced size of teeth, abnormalities of the enamel and delayed eruption (Chapter 2). However, in literature no consensus is found concerning the latter phenomenon (Wabeke and Prahl-Andersen, 1986). Bailit et al. (1968) found no significant difference in the eruption of teeth of patients with oligodontia and a control group. On the other hand Rune and Särnas (1974), evaluating tooth formation in patients with oligodontia, found a delayed tooth formation in patients with severe hypodontia. Garn and Lewis (1970) also described a delay in tooth formation in patients with third molar agenesis. Delayed tooth formation is also found in patients with multiple anomalies such as cleft palate and Down syndrome (Prahl-Andersen, 1984). Many of these syndromes also includes the congenital missing of teeth.

Several methods have been proposed for assessing dental development. Simply counting the number of teeth present in the mouth is one of these methods (Filipson and Hall, 1976). Another approach, is the rating of calcification stages of teeth (Lewis and Garn, 1960). Two methods which are commonly used are the method described by the Demirjian (1978) and the method described by Haavikko (1970).

Demirjian (1978) described eight stages of mineralization and gave each one a score. The sum of scores for an indiviudal provides an estimate of his dental maturity. The sum is converted to a dental age between 3 and 16 years.

Haavikko (1970) identified 12 radiographic stages of tooth formation for each tooth, from which for each tooth a median age and its range has been determined. The corresponding ages for all teeth present were summed and divided by the number of missing teeth, giving a mean age. Dental age is compared with the chronological age of the patient.

Anomalies in tooth size and form can be divided into anomalies of the crown and of the root. Mesiodistal dimensions of the crowns of teeth in patients with oligodontia are significantly reduced compared with mediodistal dimensions of teeth in other patients (Baum and Cohen, 1971; Chapter 5). Taurodontism and short or conical roots are reported anomalies of the roots (Oliver et al., 1975; Ruprecht et al., 1986; Seow and Lai, 1989). These short or conical roots are often described in cases with oligodontia as part of a syndrome (Oliver et al., 1975).

Taurodontism is an apical extension of the pulp chamber in a tooth with multiple roots. This phenomenon results in a proportionately shortened root and enlargement of the pulp chamber (Jorgenson, 1982). Shaw (1928) classified the following subgroups of taurodontism: hypotaurodontism, mesotaurodontism and hypertaurodontism (Fig. 6.1). Taurodontism has been observed as an isolated trait

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[1] This chapter is an edited version of two manuscripts entitled: "Tooth formation in patients with oligodontia" (authors: Schalk-van der Weide Y; Prahl-Andersen B; Bosman F), and "Taurodontism and length of teeth in patients with oligodontia" (authors: Schalk-van der Weide Y; Steen WHA; Bosman F). The first manuscript has been accepted by the Angle Orthodontist (July, 1992). The second manuscript has been accepted by the Journal of Oral Rehabilitation (Oktober, 1991). Both manuscripts are printed with permission of the publisher.

and in many syndromes, such as Klinefelter's and trisomy 21 (Down syndrome) (Ruprecht et al., 1987). It is suggested that taurodontism is the result of a disrupted developmental homeostasis (Witkop et al., 1988). Taurodontism has been of great interest to anthropologists since the first observation. It was seen as a peculiarity of ancient man, excluding Neanderthal man from the direct ancestral line of modern man (Seow and Lai, 1989; Tulensalo et al., 1989).

Criteria for the diagnosis of taurodontism differ in various studies. Both subjective and objective criteria have been used (Shaw, 1928; Tulensalo et al., 1989). Witkop et al. (1988) for example used the following reference points on radiographs: A as the lowest point of the occlusal end of the pulp chamber, B as the level at which the furcation of the roots occur and C as the position of the apex of the roots (Fig. 6.1). If AB was larger than or equal to ½ AC the tooth was considered to be taurodontic. Tulensalo et al. (1989) measured the length of a connecting line between the cemento-enamel junction to the floor of the pulp chamber on panoramic radiographs. If the distance was larger than 3.5 mm the tooth was circumscribed as being taurodontic. Variation in criteria resulted in some variation in the reported prevalence. The different rates of occurrence reported varied from 0.57% to 11.3% (Keene, 1966; Blumberg et al., 1971; Holt and Brook, 1979; Ruprecht et al., 1987).

**Figure 6.1** *Drawing of various degrees of taurodontic molars after the classification of Shaw (1928). The reference points (A,B and C) indicate the measurements as performed in the study of Witkop et al. (1988).*

Short roots have been observed in inheritable defects of tooth development such as dentinogenesis imperfecta and oligodontia. In those individuals with short roots also morphologic changes within the pulp chamber have been observed (Held and Alexander, 1985). However, although short or conical roots (Oliver et al.; 1975; Ruprecht et al., 1986) and taurodontism (Seow and Lai, 1989) are described to be associated with hypodontia, few studies have been done so far to investigate the occurrence of these abnormalities in populations of patients with oligodontia.

In the timing of a patients (orthodontic) treatment, it is important to pay attention to abnormalities in dental development. Moreover, knowledge of developmental disturbances is of importance in gaining insight in the etiology of oligodontia.

Aims of this part of the study were to evaluate i) tooth formation; ii) the occurrence of taurodontism and iii) the length of teeth in Dutch patients with oligodontia.

## 6.2 Materials and methods

*Tooth formation*

To study tooth formation data were collected of 216 patients with oligodontia (121 females and 95 males), enlisted in Departments of Oral-Maxillofacial Surgery, Prosthodontics and Special Dental Care and in private orthodontic practices throughout the Netherlands. The mean age of the patients was 11.3 years, with age range being 5 to 14 years. The group contained 6 patients with ectodermal dysplasia and 210 with isolated oligodontia. The mean number of missing teeth was 10.7 for females and 11.7 for males. A control group was derived from subjects of the Nijmegen Growth Study (Prahl-Andersen and Roede, 1979). The Nijmegen Growth Study was a longitudinal study, i.e. dental age of children was recorded more than once. In the present study, dental age of patients with oligodontia was recorded only at one age. Therefore, a sample of the Nijmegen Growth Study was used, in which every child occurred only once. The control group consisted of 443 persons (233 females and 210 males) in the age from 4 to 14 years, with a full permanent dentition.

The method used in this study was published by Demirjian (1978). He used the calcification stages of teeth as seen in panoramic radiographs to assess dental development (Fig. 6.2).

Demirjian (1978) described eight stages of development, starting from calcification of the top of the cusp to closure of the apex. It is allowed to study only one side of the arch because of the high degree of correlation which exists between the developmental stages of right and left sides of maxilla and mandible. Because of the clear view on a panoramic radiograph of mandibular teeth, all mandibular teeth on the left side were selected for the study.

Boys and girls were treated separately because of known sex differences in dental development (Demirjian, 1978; Prahl-Andersen, 1984).

**Figure 6.2** *Panoramic radiograph of a patient with oligodontia (age 11 years).*

Ratings were assigned by following the criteria described by Demirjian (1978) and by comparing the radiograph with illustrations as shown in Figure 6.3. The ratings were never based on the illustrations alone. Dental development in this study was

assessed by only one observer (YS-W).

In the Nijmegen Growth Study dental maturity scores from children in the age of 4-14 years according to the method based on Demirjian (1978) were also obtained by one observer (PB-A).

**Figure 6.3** *Calcification stages of a molar after the ratings developed by Demirjian (1978), as given by Prahl-Andersen and van der Linden (1972). Copied with permission of the editor.*

*Taurodontism and length of teeth*

For this part of the study 117 panoramic radiographs of patients with oligodontia (62 females and 55 males) were collected, of which 90 (46 males and 44 females) were suitable for assessing taurodontism. The mean age was 20 years, with age range being 12 to 37 years. The patients were enlisted in Departments of Oral-Maxillofacial Surgery, Prosthodontics and Special Dental Care and a Department of Orthodontics in the Netherlands. Oligodontia as part of a syndrome was diagnosed in 16 patients. Fourteen of them had ectodermal dysplasia, one patient had the Bloch-Sulzberger syndrome and one patient had Ectrodactyly- Ectodermal dysplasia-Clefting-syndrome. The other 111 patients had isolated oligodontia.

Panoramic radiographs of 91 control persons (40 males and 51 females) were collected. The mean age was 20 years, with age range being 14 to 35 years. They were all healthy persons enlisted in the Department of Oral-Maxillofacial Surgery, Prosthodontics and Special Dental Care in Utrecht. They had a full permanent dentition and did not suffer from any defects which may be associated with oligodontia.

The method used to assess taurodontism was based on the method described by Seow and Lai (1989). The procedure was as follows: First the outline of the mandibular first molar was traced from the panoramic radiograph. The following parts of the molar were identified: a) the crown plus body (CB) and b) the root (R). The CB of the tooth was determined by drawing a line through the deepest pit which was parallel to the occlusal line joining the highest cusps (Fig. 6.4). A vertical line

was drawn at right angles to the occlusal line. The length of CB was determined as the distance between the deepest pit and the furcation, and measured along the vertical line. The length R was determined along the same line from the furcation to the apex of the root (Fig. 6.4). In this study the length R was defined as the length along the vertical axis from the furcation to the apex of the longest root. Seow and Lai (1989) used the CB:R ratio to classify three types of taurodontism as described by Shaw (1928) (Fig. 6.1). A molar was classified as hypotaurodont if the CB:R ratio was within the range 1.10-1.29. Mesotaurodontism was defined as a CB:R ratio within the range of 1.30-2.00 and hypertaurodont if the ratio was larger than 2. When the CB:R ratio was less than 1.10 the molar was considered as being normal. In this study, patients were classified as taurodont if at least one of the mandibular first molars was taurodontic. We selected the mandibular first molar for this study because from an earlier part of the study it appeared that the mandibular first molar is most often present in patients with oligodontia (Chapter 4). The entire outline of the crown and the roots of the mandibular first molar is also clearly visible on the panoramic radiographs. Using the method of Seow and Lai (1989) allowed us to compare the results of both studies. It was the only study known of in which the occurrence of taurodontism in patients with hypodontia was evaluated.

**Figure 6.4** *Measurements as performed on a mandibular first molar to assess the presence of taurodontism, according to the method of Seow and Lai (1989). CB is the Crown-Body and R the length of the roots.*

**Figure 6.5** *Measurement of the length as performed on canines and premolars.*

Length of the following teeth were measured: canines, premolars and first molars of the mandible. The length of the molar was identified as the distance between the line joining the highest cusps to the apex of the longest root (Fig. 6.4). The length of the canines and premolars were identified as the distance between the highest cusp to the root apex (Fig. 6.5).

To study the length of teeth from radiographs we have to bear in mind that panoramic radiographs may be associated with distortions (Sanderink, 1987). Van Aken (1973) calculated the horizontal and vertical magnification in a theoretical model. The vertical magnification is defined as the result of focus-film distance divided by focus-object distance (Sanderink, 1987). According to van Aken (1973) the vertical magnification, of a palomex$^{R}$ orthopantomograph was 1.33 $\pm$ 0.06

assuming that the patient stays within 15 mm in or out "the plane in focus". Therefore, the real length on a panoramic radiograph, of a palomex$^R$ orthopantomograph, can be obtained by multiplying the measured length by 3/4 (100/133). For other orthopantomographs other magnification factors were found.

In this study, all measurements from panoramic radiographs were corrected for the magnification factor of the equipment used, 1.20 $\pm$ 0.04 for the panelipse$^R$, GCE$^R$ (Manson-Hing, 1985) and 1.33 $\pm$ 0.06 for the palomex$^R$, Siemens (van Aken, 1973).

*Inter-observer agreement and error analysis*

In order to calculate the inter-observer agreement dental age was assessed on 20 panoramic radiographs by the two observer's (YS-W; BP-A). Cohen's Kappa was calculated. Cohen's Kappa is a measure of agreement of two or more observers after agreement due to chance is excluded (Landis and Koch, 1977).

Errors inherent to assessing taurodontism and measuring the length of teeth, can be divided in radiographic errors and measuring errors (Steen, 1984). Radiographic errors can be divided into errors due to processing of the radiograph (non-geometric errors) and geometric errors e.g. magnification and distortion. Measuring errors are due to differences in interpretation of panoramic radiographs by observers (Ramstad et al., 1978).

The total error for determining the length of teeth was defined as:

$s^2_{tot\ (length)} = s^2_{measurements} + s^2_{radiograph}$

For calculating $s^2_{measurements}$ 20 panoramic radiographs were scored on two different moments by two observers. Measurements were performed according to a clear protocol. The following formula was used to calculate the total measuring error:

$s^2_{measurements} = s^2_{intra\text{-}observer} + s^2_{inter\text{-}observer}$ (1)

The intra-observer error was estimated from duplo measurements from observer A and B: $s^2_{intra\text{-}observer} = (s^2_{(A)} + s^2_{(B)})/2$ (2)

The $s^2_{(A,B)}$ were calculated using the following formula: $s^2_{intra\text{-}observer} = \Sigma d_i^2/2N$ (3)

The variance of one observation is $s^2$, $d_i$ is the difference between the two outcomes of the i'th pair of observations by one observer and N is the number of pairs (Jonge de, 1964). The difference calculated was the difference between the length of a teeth as measured the first time by observer A (B) and the length of a teeth measured by observer A (B) on the second time. The $s^2_{intra\text{-}observer}$ was 0.18 mm. Formula 3 was also used to calculate the inter-observer error. The difference $d_i$ was defined as the difference between the mean of the two measurements of observer A and the mean of the two measurements of observer B. The $s^2_{inter\text{-}observer}$ was 0.20 mm, therefore, the total measuring error was according to formula 1:

$s^2_{measurements} = 0.20 + 0.18 = 0.38$ mm. A correction for the magnification factor was made.

The standard deviation of the vertical magnification as calculated by van Aken (1973), for the different types of radiographic equipment, was used to define the $s^2_{radiograph}$. The maximal error of the magnification factor, used in this study, was 4.5%. Therefore, the maximal $s^2_{radiograph}$ can be defined as 4.5% of the maximal measured length. Using the maximal measured length, which was 30 mm, the maximal total error in determining the length of teeth was:

$s^2_{tot\ (length)} = s^2_{measurements} + s^2_{radiograph}$ ---> $2.2025 = 0.38 + (30 \times 0.045)^2$

In determining taurodontism the ratio of the measured length of CB and R was used. The length of CB as well as the length of R have a $s^2_{radiograph}$ of 4.5%. Since the ratio CB:R was used in this study the $s^2_{radiograph}$ has no influence. The total error equals the $s^2_{measurements}$. The formulas 1,2 and 3 mentioned above were used to calculate the total measuring error for assessing taurodontism. The intra-observer error was 1.7 $10^{-5}$ and the inter-observer error was 8.6 $10^{-3}$. The $s^2_{measurements}$ (and therefore the maximal total error) was 8.62 $10^{-3}$.

*Statistical procedure*

The differences in tooth formation between patients with oligodontia and normal patients were evaluated by means of a logistic regression technique (Hosmer and Lemeshov, 1989) which was applied to groups separately for each stage.

Logistic regression is a regression technique for estimating the probability that a tooth has reached a certain stage of formation, depending on the values of one or more covariables like age, sex and so on. Tests are available to determine which covariables contribute significantly to the model. Age, sex and group were significant covariables. Therefore, the two groups (oligodontia and controls) were treated separately for both males and females. The logistic regression models were used to calculate the 50% points (median) for the various stages for all tooth. The 50% points represent the point where 50% of the patients had reached the stage in question. The differences between the 50% points (median) of patients with oligodontia and the data from the Nijmegen Growth Study were studied (Finney, 1978).

For evaluating the difference in length of teeth between patients with oligodontia and normal patients, the statistical procedure was as follows: i) a Kolmogorov-Smirnov test was performed to evaluate the normality of the distribution of the collected data; ii) an F-test was performed to test whether the standard deviations of both populations could be assumed equal; iii) if the standard deviations could be assumed equal a Student's t-test for comparison of two means was used. In case the standard deviations couldn't be assumed equal a Welch's test for comparisons involving two variations, which must be separately estimated was used.

Chi-square tests were used to determine significant difference in the case of taurodontism (Harnett, 1982).

## 6.3 Results

### 6.3.1 Dental age

The inter-observer agreement was calculated by means of a Cohen's Kappa which resulted in a Cohen's Kappa of 0.65. The weighted kappa was 0.71.

The results of the logistic regression models - the 50% or median points - are summarized in the Tables 6.1 and 6.2. There was a tendency in males for teeth to show delayed dental development in the early stages compared with the control group. In the last three stages the delay was less evident. In males for stage 5 of the lower second molar, the first and second premolar and the canine and for the fourth

stage of the lower second molar significant differences were found between the 50% points of patients with oligodontia and the control group.

**Table 6.1** *The 50% points (median) ± standard error of the curves constructed with logistic regression, for both males with oligodontia (O) and the control group (N). The 50% point represent the age at which 50% of the persons are in calcification stage 1 thru 4, 1 thru 5 and so on.*

| Stage<br>Tooth | 1 thru 4 | 1 thru 5 | 1 thru 6 | 1 thru 7 |
|---|---|---|---|---|
| 37 O | 10.5 ± 0.45* | 12.2 ± 0.26* | 13.9 ± 0.51 | - |
| 37 N | 9.0 ± 0.20 | 10.8 ± 0.18 | 13.3 ± 0.15 | - |
| 36 O | - | - | 7.9 ± 0.64 | 11.2 ± 0.25 |
| 36 N | - | - | 8.5 ± 0.18 | 10.9 ± 0.16 |
| 35 O | 9.8 ± 0.53 | 12.1 ± 0.61* | - | - |
| 35 N | 9.2 ± 0.19 | 10.4 ± 0.18 | - | - |
| 34 O | 8.3 ± 0.58 | 10.8 ± 0.25* | 13.2 ± 0.44* | 14.3 ± 0.44* |
| 34 N | 8.5 ± 0.19 | 9.9 ± 0.16 | 12.0 ± 0.15 | 13.3 ± 0.19 |
| 33 O | 7.3 ± 0.74 | 10.4 ± 0.24* | 12.6 ± 0.43 | 14.1 ± 0.61 |
| 33 N | 7.8 ± 0.19 | 8.9 ± 0.16 | 11.7 ± 0.14 | 14.1 ± 0.25 |

**Legend Tables 6.1 and 6.2:**
O = Oligodontia; N = Nijmegen Growth Study; * = $P < 0.05$

**Table 6.2** *The 50% points (median) ± standard error of the curves constructed with logistic regression, for both females with oligodontia (O) and the control group (N). The 50% point represent the age at which 50 % of the persons are in calcification stage 1 thru 4, 1 thru 5 and so on.*

| Stage<br>Tooth | 1 thru 4 | 1 thru 5 | 1 thru 6 | 1 thru 7 |
|---|---|---|---|---|
| 37 O | 8.3 ± 1.22 | 11.6 ± 0.51* | 13.0 ± 0.28 | - |
| 37 N | 8.8 ± 0.18 | 10.4 ± 0.15 | 12.9 ± 0.14 | - |
| 36 O | - | - | 7.8 ± 0.69 | 10.1 ± 0.28 |
| 36 N | - | - | 8.0 ± 0.15 | 10.4 ± 0.15 |
| 35 O | - | 9.8 ± 1.12 | 13.5 ± 0.60 | - |
| 35 N | - | 10.1 ± 0.15 | 12.4 ± 0.12 | - |
| 34 O | 7.9 ± 0.75 | 9.8 ± 0.40 | 12.0 ± 0.24 | 13.2 ± 0.26 |
| 34 N | 7.7 ± 0.19 | 9.3 ± 0.17 | 11.6 ± 0.12 | 12.9 ± 0.17 |
| 33 O | 6.8 ± 1.10 | 8.6 ± 0.39 | 10.8 ± 0.24 | 13.0 ± 0.38 |
| 33 N | 7.0 ± 0.18 | 8.1 ± 0.15 | 11.0 ± 0.12 | 13.1 ± 0.21 |

Furthermore, significant differences were found for the sixth and seventh stage of the first premolar (Table 6.1).

In females only stage 5 of the lower second molar differed significantly comparing patients with oligodontia and controls (Table 6.2).

### 6.3.2 Taurodontism

The results of the occurrence of taurodontism are summarized in the Tables 6.3-6.8.

**Table 6.3** *The occurrence of taurodontism in patients with oligodontia and a control group.*

| | Taurodontism | | | |
|---|---|---|---|---|
| | Present | | Absent | |
| Patients with oligodontia N = 90 | 26 | 28.9 % | 64 | 71.1 % |
| Control group N = 91 | 9 | 9.9 % | 82 | 90.1 % |

$X^2 = 10.5$ ($P < 0.01$)

**Table 6.4** *The occurrence of taurodontism in mandibular first molars.*

| | Taurodontism | | | |
|---|---|---|---|---|
| | Present | | Absent | |
| Patients with oligodontia Number of first molars = 170 | 37 | 21.8 % | 133 | 78.2 % |
| Control group Number of first molars = 182 | 13 | 7.1 % | 169 | 92.9 % |

$X^2 = 15.51$ ($P < 0.001$)

In Table 6.3 the occurrence of taurodontism in patients with oligodontia and the control group is given. Patients and controls were classified as taurodont if the CB:R ratio of one or two mandibular first molars was larger than or equal to 1.10. In Table 6.4 the number of taurodontic mandibular first molars is given. In some patients with oligodontia one of the two mandibular first molars was congenitally missing. In patients with oligodontia the prevalence of taurodontism was significantly higher than in the control group (Tables 6.3 - 6.4). There was no significant difference in the distribution over males and females in both groups. No significant sex difference was found within the two groups (Table 6.5). Neither was there a significant difference between unilateral and bilateral occurrence of taurodontism (Table 6.6). The mesotaurodont and hypertaurodont molars were found especially in the group of patients with oligodontia (Table 6.7). Table 6.8 shows the range of the CB:R ratio for the normal mandibular first molars for males and females patients and controls. No significant differences were observed between the mean ratios of normal patients with exception of the ratio of the mandibular left first molar of males.

**Table 6.5** *The occurrence of taurodontism in males and females.*

| | Patients with oligodontia | | Control group | |
|---|---|---|---|---|
| Taurodontism: | Present | Absent | Present | Absent |
| Males | 14 | 32 | 5 | 35 |
| Females | 12 | 32 | 4 | 47 |

$X^2_{\text{control-oligodontia}} = 7.9\ 10^{-3}$ $(P > 0.01)$
$X^2_{\text{control (males-females)}} = 0.5$ $(P > 0.01)$
$X^2_{\text{oligodontia (males-females)}} = 0.11$ $(P > 0.01)$

**Table 6.6** *The unilateral and bilateral occurrence of taurodontism.*

| | Taurodontism | | |
|---|---|---|---|
| | Unilateral | | Bilateral |
| Patients with oligodontia | 15 | (8 L/ 7 R) | 11 |
| Control group | 5 | (3 L/ 2 R) | 4 |

$X^2 = 0.012$ $(P > 0.01)$

**Table 6.7** *The distribution of the types of taurodontism (hypotaurodont, mesotaurodont and hypertaurodont) in patients with oligodontia and the control group.*

| | Taurodontism | | |
|---|---|---|---|
| | Hypotaurodont 1.10 - 1.29 | Mesotaurodont 1.30 - 2.00 | Hypertaurodont > 2.00 |
| Patients with oligodontia | 26 | 9 | 2 |
| Control group | 12 | 1 | 0 |

### 6.3.3 Length of teeth

The results regarding the length of teeth are summarized in Table 6.9. In males only the right lower first molar was significantly reduced whereas in females the canines and lower first molars were significantly reduced in length (Table 6.9).

In patients with oligodontia 10.8% of the mandibular first molars, classified as taurodontic, also showed a reduced length (Table 6.10). In those cases the length was considered to be reduced when the length was less than the mean length minus the standard deviation and minus the total error.

**Table 6.8** *The range and mean of the CB:R ratio of normal mandibular first molars.*

| | | 36 | | 46 | |
|---|---|---|---|---|---|
| | | Range CB:R | X ± SD | Range CB:R | X ± SD |
| Control group | Males | 0.62 - 1.07 | 0.84 ± 0.11 | 0.55 - 1.07 | 0.86 ± 0.12 |
| | Females | 0.67 - 1.02 | 0.84 ± 0.08 | 0.54 - 1.07 | 0.87 ± 0.12 |
| Patients with oligodontia | Males | 0.60 - 1.02 | 0.91 ± 0.13 | 0.60 - 1.07 | 0.90 ± 0.12 |
| | Females | 0.64 - 1.08 | 0.88 ± 0.13 | 0.63 - 1.09 | 0.88 ± 0.12 |

**Table 6.9** *Length of mandibular teeth of females and males.*

| Tooth | N1 | X1 | SD | N2 | X2 | SD | N3 | X3 | SD | N4 | X4 | SD |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 33 | 40 | 22.1 | 2.2 | 47 | 23.4 | 1.9* | 27 | 23.8 | 3.8 | 39 | 25.2 | 2.2# |
| 34 | 35 | 21.0 | 1.9 | 49 | 21.7 | 1.7# | 34 | 22.2 | 2.0 | 40 | 22.7 | 2.2# |
| 35 | 14 | 21.0 | 2.2 | 50 | 22.3 | 2.2# | 14 | 22.9 | 2.3 | 40 | 23.5 | 1.9# |
| 36 | 39 | 20.1 | 1.9 | 51 | 21.9 | 1.4* | 33 | 21.2 | 2.3 | 40 | 21.9 | 1.5# |
| 43 | 36 | 22.1 | 1.7 | 48 | 23.2 | 2.1* | 25 | 24.6 | 2.8 | 36 | 25.5 | 2.5# |
| 44 | 34 | 21.0 | 1.9 | 47 | 21.6 | 2.0# | 35 | 22.1 | 2.5 | 38 | 22.5 | 1.9# |
| 45 | 11 | 22.0 | 2.3 | 49 | 22.0 | 2.2# | 18 | 22.1 | 3.1 | 38 | 23.5 | 1.6# |
| 46 | 33 | 19.8 | 2.4 | 51 | 21.4 | 2.9* | 29 | 21.0 | 2.1 | 40 | 22.3 | 1.6* |

**Legend Table 6.9:**

X1; X2 = mean length (in mm) of teeth of females
X3; X4 = mean length (in mm) of teeth of males
SD = standard deviation
# = P > 0.01
N1; N3 = sample size of oligodontia
N2; N4 = sample size of the control group
* = P < 0.01

**Table 6.10** *The simultaneous occurrence of taurodontism and a reduced length in mandibular first molars.*

| Number of first molars | | Taurodontism / Length | Taurodontism |
|---|---|---|---|
| Patients with oligodontia | N=37 | 4 (10.8 %) | 33 |
| Control group | N=13 | 0 (0 %) | 13 |

## 6.4 Discussion

*Dental age*

In patients with oligodontia, a tendency for teeth to show delayed tooth formation was observed. The delay was more obvious in males than in females. Unfortunately, the present material did not permit an evaluation of the first three stages, because no panoramic radiographs were available. Reason for this is that patients with

oligodontia are often not diagnosed as having congenitally missing teeth until the age of 11-12 years. Most often at that age the patients are referred to an orthodontic practitioner for the first time.

Reasons for not choosing the method of counting the teeth as a measure of dental age were the following: In humans considerable variation exists in time of eruption of permanent teeth. The emergence of teeth is also disturbed by several exogenous factors such as infection, premature extraction of a deciduous tooth and other local factors. The method based on the use of clinical emergence is limited to certain periods, no teeth erupts from 8 to 10 years of age and after the 12th year. Disadvantages related to counting the number of teeth in the mouth to assess dental development do not play a role in using calcification stages of the teeth as seen on panoramic radiographs. Using the method of Demirjian (1978) allowed us to compare our results to those of the Nijmegen Growth Study (Prahl-Andersen and Roede, 1979). The inter-observer agreement was considered as satisfactory (Cohen's Kappa = 0.65), so a reliable comparison was possible.

In different methods rates of calcification of the different teeth are commonly used to calculate dental age, which is then compared with the chronological age. For computing dental age according to the method of Demirjian (1978), it is necessary to rate all four or all seven left or right mandibular teeth. In the present study, it was not possible to compute dental age because of the congenitally missing teeth. In each individual different teeth are missing which makes it impossible to calculate dental age. Moreover, a difference in delay for the different types of teeth could be missed using dental age. Therefore, in this study logistic regression models were constructed of all stages for each tooth. The points at which 50% of the patients with oligodontia had reached a certain stage of tooth formation were compared with the 50% points calculated of the control group (Tables 6.1 and 6.2). Standard errors of the 50% points were calculated.

In a study of patients with severe hypodontia (i.e. missing four or more teeth) delayed tooth formation was described by Rune and Särnas (1974). They calculated the mean age of individual formation stages of the teeth, according to the method of Haavikko (1970). The mean delay was 2.0 years in males and 1.8 years in females. In general the delay was more severe in the early stages. Those findings of Rune and Särnas (1974) are in concordance with the findings of males in the present study. However, although in the present study the patients were missing six or more teeth, the delay was less pronounced. Significant differences between patients with oligodontia and the control group in the 50% points (median) of the logistic regression models were found in only a few stages. In males, the fifth stage of second lower molar, first and second lower premolar and canine differed significantly as well as the fourth stage of the lower second molar. Furthermore, the sixth and seventh stage of the lower first premolar were significantly different compared with the control group. In females, stage 5 of the lower second molar showed a significant difference. In some teeth the logistic regression model also showed a significant interaction between age and group, indicating different curves of tooth formation for that tooth of patients with oligodontia and children of the Nijmegen Growth Study.

The higher standard errors of the 50% points of the patients with oligodontia compared with those of the control group (Tables 6.1 and 6.2) could be due to the

distributions of persons of the control group and of the patients with oligodontia over the stages. The range of the age of the patients in one stage is comparable. However, in patients with oligodontia a tendency for a levelled distribution was found, i.e. equal numbers of individuals whom are in the same stage of tooth formation were found in different age groups. In the control group a tendency for a peak distribution was found, i.e. the highest number of individuals whom were in the same stage was found at a certain age group. In the surrounding age groups lower number of individuals were found.

Garn and Lewis (1970) described a posterior-anterior gradient of delay in tooth formation timing. In our study no such gradient was found. Rune and Särnas (1974) could also not ascertain such a gradient.

Several other studies report a delay of tooth formation in cleft lip/ palate patients with and without hypodontia (Ranta, 1984b; Ranta, 1986). In those studies dental age of patients was compared with chronological age. The mean delay in tooth formation in cleft affected children varies from 0.3 to 0.7 years (Ranta, 1986). Prahl-Andersen (1976) reported a tendency in children to show a delayed tooth formation until the age of 9 years. However, in a later study no difference was found in females with or without clefts. The formation was delayed in boys with clefts (Prahl-Andersen, 1979). These findings are in agreement with the findings in the present study, where also tooth formation was more severely delayed in the early stages. The delay was more obvious in males than in females. Ranta (1984b) described, in contrast with the previous findings, a significantly longer delay in the older age group.

Harris and Hullings (1990) reported the delay in tooth formation in patients with isolated cleft lip/palate to be more severe in early-developing teeth (M1, C) than in late-developing teeth (M2, M3). Those results were not confirmed in our study. Harris and Hullings (1990) described an asymmetry in development of teeth in isolated cleft lip/palate patients. In the present study, no asymmetry in tooth development was found in either patients or controls. Even the teeth which were most likely to be congenitally missing (35, 45) showed no asymmetry in tooth development. Probably the differences in asymmetry found in development of teeth can be explained by the differences in distribution of missing teeth. In the study of Harris and Hullings (1990) 35 patients had unilateral clefts. It is known that in patients with unilateral cleft lip/ palate the distribution of the upper missing teeth is often asymmetric (Ranta, 1986). Rune and Särnas (1974) reported a marked delay of the contralaterals to missing teeth. Apparently, the distribution of missing teeth was asymmetric. In the present study, there was a high degree of symmetry in the distribution of missing teeth in both lower and upper jaw. This could explain the symmetry found in development in our study in contrast with the findings of Harris and Hullings (1990) and Rune and Särnas (1974).

*Taurodontism and length of teeth*

There have been some case reports which described the occurrence of taurodontism in cases with oligodontia (Milazzo and Alexander, 1982; Gorlin et al., 1990). However, to the author's knowledge, except for Seow and Lai (1989) no other studies so far described the occurrence of taurodontism in patients with oligodontia. The present sample of patients with oligodontia shows that taurodontism

of one or two first mandibular molars occurs in 28.9% of the patients. These findings are in agreement with those of Seow and Lai (1989). The group of patients evaluated in the study of Seow and Lai (1989) consisted of patients with the congenital missing of one or more teeth. However, 56.5% of their patients with taurodontism had congenitally missing six or more teeth. Unfortunately, they did not mention the percentage of patients with congenitally missing six or more teeth in the group as a whole. As in the study of Seow and Lai (1989) no sex difference and no difference between unilateral and bilateral occurrence of taurodontism was observed in the present study.

The prevalence of taurodontism in our study on normal Dutch subjects was 9.9%. Compared with other studies of caucasian populations this is a high percentage. However, interpretation of the rates of occurrences from literature is difficult because authors do not always state clearly whether the reported frequency is per individual in the population or per tooth in a sample of teeth. For white americans the prevalence of taurodontism is reported to vary from 2.5 to 3.2% (Witkop et al., 1988). In this study 7.1% of the mandibular first molars were classified as taurodontic. This percentage is more within the range of the reported prevalences. Holt and Brook (1979) for example reported an incidence of 6.3 % in mandibular first molars in a sample of British schoolchildren.

An error analysis was performed to analyze the maximal error in measuring the length of teeth. For the different types of teeth the standard deviation was approximately 10%. As shown in the error analysis the maximal radiographic error was 4.5% and the $s^2_{measurements}$ was 0.38 mm. This allowed us to classify an individual as having a reduced length when the length was 2.20 mm less than the mean length for the concerning group. The difference of 2.20 mm is within the range of the standard deviations of the length of teeth as found in both the control group and the patients with oligodontia. Therefore, we considered the method used as appropriate. Measurements by only one observer would have been sufficient.

In this study, the length of the canines and first molars of females and of the lower right first molar in males were significantly reduced. The premolars were not significantly reduced in both males and females. The differences found were less than 2 mm. It can be expected that such a small difference has no clinical relevance. Because of the method used in the present study, it was not possible to determine if the reduction was a reduction in height of the crown or a reduction in length of the roots.

To the author's knowledge, no studies have been performed to measure the length of teeth in patients with oligodontia, although short or conical roots are reported in cases with oligodontia as part of a syndrome (Oliver et al., 1975; Ruprecht et al., 1987). In our study only two patients with a reduced length of the mandibular first molar had oligodontia as part of a syndrome.

The etiology and pathogenesis of taurodontism is still unclear. The consensus is however, that taurodontism results from a developmental disturbance in Hertwig's epithelial root sheath. It is suggested that the defect is ectodermal in origin (Jorgenson, 1982; Jorgenson et al., 1982). According to Witkop et al. (1988) the mechanism by which taurodontism occurs may be related to disruption and slowing of cell growth cycles. A failure of delay of the ectomesenchyme to induce epithelium of the root sheath, or failure of the response of the epithelium could result in a delay

in the morphogenesis of roots of teeth. In many of the syndromes, of which oligodontia is one of the features, ectodermal defects are involved (Gorlin et al., 1990). The present findings, therefore, support the hypothesis that a defect in ectodermal cells may be involved in taurodontism. The results of Witkop et al. (1988) in the study of the occurrence of taurodontism in patients with X-chromosomal aneuploidy and Down syndrome, support the concept that chromosomal abnormalities disrupt the developmental homeostasis of tooth form and that taurodontism is not the result of specific genes on the chromosomes involved. The association of oligodontia and an increase of the prevalence and severity of taurodontism, therefore, may be a manifestation of developmental instability in patients with oligodontia.

Of the patients with oligodontia 10.8% of the mandibular first molars classified as taurodontic also showed a reduced length of the teeth. Hertwig's epithelial root sheath is the architect of the root, as the length, curvature and thickness and number of roots are dependent on this cell layer and the adjacent (ecto-)mesenchymal cells. (Avery, 1987). Therefore, reduced length of teeth may also be the result of a defect in ectodermal cells, which resulted in a defective root formation. The simultaneous occurrence of taurodontism and a reduced length in mandibular first molars and occurrence of a reduced length in patients with oligodontia support this hypothesis. However, further studies are necessary to confirm this hypothesis and to evaluate possible association of a reduced length and taurodontism.

Little attention has been paid so far to the clinical relevance of taurodontism and a reduced length of teeth. Durr et al. (1980) reported that taurodontism didn't interfere with amalgam restorations. However, endodontic therapy may be more difficult. Locating of the orifices of the pulp canals and instrumentation cause problems because of the shape of the pulp chamber. No information has been given so far, about which influence taurodontism and a reduced length of teeth has on prosthetic therapy, orthodontics and about the use of taurodontic / reduced teeth as abutment teeth. A tooth with a reduced length or taurodontic shape may not have as much stability and strength as a normal abutment teeth. One should take in consideration the increase of vertical dimension, which is often part of dental treatment of patients with oligodontia. This increase of vertical dimension is unfavourable for the crown-root ratio. Specially in case of extensive bridgework this crown-root ratio is of great importance. In the situation of an unfavourable crown-root ratio the bridgework is likely to fail rapidly. No research has been done so far to investigate the prognosis of those unfavourable ratios using various types of dental therapy.

## 6.5 Conclusions

The results of this study, indicated that there is a great individual variation in tooth formation between patients with oligodontia. Some patients with oligodontia showed a severely delayed tooth formation whereas others showed a normal tooth formation, in contrast with the control group of whom tooth formation of the individuals stayed within the normal biological variation. Therefore, tooth formation of each patient with oligodontia should be individually examined before starting treatment.

It can be concluded, taken into account the number of observations of each stage, that there is a delay in tooth formation of patients with oligodontia compared with the control group. This delay was more obvious in males than in females.

Furthermore it can be concluded from the present study that patients with oligodontia more often have taurodontic molars and a reduced length of teeth than controls.

More attention should be paid to these clinical aspects of taurodontism and a reduced length of the teeth. The general practitioner should evaluate the size and development of the teeth of patients with oligodontia carefully before starting dental treatment.

# Chapter 7
# Oral and extra-oral symptoms and associations between combinations of these symptoms[1]

## 7.1 Introduction

A syndrome is "a pattern of multiple anomalies thought to be pathogenetically related and not known to represent a single sequence or a polytopic field defect" (Spranger et al., 1982). The word syndrome is derived from Greek and means "a running together" (Cohen, 1989). Identification of a syndrome in a patient with multiple anomalies is a major diagnostic problem. However, diagnosis is essential for effective patient management: treatment, prognosis and genetic counselling (Hall, 1983).

So far, congenitally missing teeth have been described as one of the features in more than 120 syndromes (Appendix 1). In some of these syndromes oligodontia is a significant and integral diagnostic feature while in others oligodontia is merely described as an associated finding.

One of the syndromes in which oligodontia is a key feature is hypohidrotic ectodermal dysplasia. This syndrome is characterized by the triad hypohidrosis, hypotrichosis and congenitally missing teeth (Gorlin et al., 1990). Another syndrome in which oligodontia is an important feature is Rieger syndrome. The major features of this syndrome are congenitally missing teeth, malformation of the anterior chamber of the eye and umbilical anomalies (Gorlin et al., 1990).

Some syndromes have particular patterns of congenitally missing teeth (Jorgenson, 1980). Knowledge of the existence of specific patterns of congenitally missing teeth can contribute to an early diagnosis. Patients with Rieger syndrome for example often have agenesis of the permanent upper and lower central and lateral incisors. If the permanent lower incisors are present they are often conically shaped (Childers and Wright, 1986). Böök's syndrome can also be recognized on the basis of a specific pattern of congenitally missing teeth. In Böök's syndrome an association is present of agenesis of permanent upper and lower premolars with premature whitening of the hair and increased sweating (Jorgenson, 1980). Table 7.1 shows a list of syndromes known with specific patterns of congenitally missing teeth.

For a general practitioner it is nearly impossible to be aware of all the symptoms associated with the many syndromes which can possibly occur in patients with oligodontia. However, to establish an early diagnosis and to be able to distinguish between oligodontia/I and oligodontia/S, it is important for a general practitioner also to have knowledge of the characteristics of oligodontia. The differentiation between oligodontia/I and oligodontia/S is a prerequisite for genetic counselling. In the case of congenitally missing teeth as part of a syndrome the recurrence risk can be quite different from that of the isolated type. Besides, the number and severity of symptoms is - per definition - higher.

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[1] This chapter is an edited version of the manuscript entitled: "Symptomatology of patients with oligodontia" (authors: Schalk-van der Weide Y; Beemer FA; Faber JAJ; Bosman F), which is accepted by the Journal of Oral Rehabilitation (August, 1992), and which is printed with permission of the publisher.

The aim of this part of the study was to identify the association of specific patterns of congenitally missing teeth with specific combinations of extra-oral symptoms.

**Table 7.1** *Syndromes with more or less specific patterns of congenitally missing teeth.*

| Syndromes | Mode of inheritance | Pattern of congenitally missing teeth |
|---|---|---|
| Böök's syndrome (PHC syndrome+) | AD* | Premolars |
| Rieger syndrome | AD* | Maxillary incisors (constant), mandibular incisors and premolars (occasional) |
| Ellis-Van Creveld syndrome | AR** | Mandibular incisors and canines |
| Gorlin-Chaudry-Moss syndrome | AR** | Deciduous molars, secondary premolars and molars |
| Lipoid proteinosis | AR** | Maxillary lateral incisors, canines and premolars |
| Coffin-Lowry syndrome | X-Linked recessive | Maxillary lateral incisors, mandibular incisors |
| Orofaciodigital syndrome Type I | X-linked dominant | Mandibular incisors and canines |
| Cleft lip/palate | Multi-factorial[1] | Maxillary lateral incisors and canines |
| Down syndrome | Chromo-somal | Third molars, mandibular second premolars, and maxillary lateral incisors |
| Holoprosencephaly | Various[2] | Maxillary incisors |
| Hypoglossia-hypodactylia syndrome | Sporadic | Mandibular incisors and canines |
| Glossopalatine ankylosis syndrome | AD* | Incisors |

**Legend Table 7.1:**
+ = Premolar aplasia- Hyperhidrosis- Canities prematura
* AD = autosomal dominant; ** AR = autosomal recessive
1: Also mendelian inheritance patterns are described
2: Several modes of inheritance are described

## 7.2 Materials and methods

In this study, 167 patients with oligodontia were interviewed and documented, as described in Chapter 3. The group consisted of 83 males and 84 females (mean age 24 years, with age range being 3 to 54 years). The patients were enlisted in Departments of Oral-Maxillofacial Surgery, Prosthodontics and Special Dental Care in various regions of the Netherlands.

Of these 167 patients, 48 patients had oligodontia/S, 89 patients had oligodontia/I and 30 patients had oligodontia/I-S. The syndromes occurring in patients with oligodontia/S are listed in Table 7.2.

**Table 7.2** *Syndromes associated with oligodontia (present study).*

| | Number of patients |
|---|---|
| Ectodermal dysplasia | 41 |
| Rieger syndrome | 1 |
| Ectrodactyly-Ectodermal dysplasia-Clefting (EEC) syndrome | 2 |
| Bloch-Sulzberger syndrome | 2 |
| Cutis marmorata teleangiectatica congenita | 1 |
| Oto-palato-digital syndrome (Type I) | 1 |

Symptoms occurring in patients with oligodontia/I were compared with symptoms occurring in a control group. This group consisted of 135 healthy controls with a full permanent dentition (59 males and 76 females; mean age 21 years, with age range being 7 to 54 years). The persons were interviewed on several locations in the Netherlands. Persons with congenitally missing teeth were excluded from the control group. Persons with family members with congenitally missing teeth were also excluded. The group was matched for race, sex and age.

Combinations of extra-oral symptoms were derived using the following symptoms: skin, hair, nails, sweat and tear secretion, and are presented in Table 7.3. The patterns of congenitally missing teeth are presented in Table 7.4.

*Statistical analysis*

Chi-square tests and a test on the difference between two proportions were used looking for differences between combinations of extra-oral symptoms (Table 7.3); patterns of congenitally missing teeth (Table 7.4); the extra-oral symptoms separately and the congenitally missing teeth (Harnett, 1982). The significance level for this study was set on 0.01. The same analyses were performed to examine if there were any significant differences between patients with oligodontia/I and the control group. Additionally, correspondence analysis and logistic regression were performed to evaluate differences between patients with oligodontia/S and oligodontia/I and differences between the control group and patients with oligodontia/I.

Correspondence analysis (Greenacre, 1984) was used to illustrate the differences between the three groups of patients - oligodontia/I, oligodontia/S and the control group - concerning the distribution of the combinations of extra-oral symptoms, and the relationship between the total number of missing teeth and the combinations of extra-oral symptoms.

Correspondence analysis is a technique which allows exploratory examination of the relationship between variables in a multidimensional space, like principal component analysis for continuous data.

**Table 7.3** *Combinations of extra-oral symptoms.*

| | C 1 | C 2 | C 3 | C 4 | C 5 | C 6 | C 7 | C 8 | C 9 | C 10 | C 11 | C 12 | C 13 | C 14 | C 15 | C 16 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Skin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Hair | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Nails | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| Swsec* | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 |
| Tesec# | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 |

| | C 17 | C 18 | C 19 | C 20 | C 21 | C 22 | C 23 | C 24 | C 25 | C 26 | C 27 | C 28 | C 29 | C 30 | C 31 | C 32 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Skin | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Hair | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Nails | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| Swsec* | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 |
| Tesec# | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 |

**Legend Table 7.3:**
For all symptoms, skin - hair - nails - sweat secretion and tear secretion:
0 = abnormality of the concerning symptom and 1 = normality of the concerning symptom

For example pattern C12 consist of a patient with an abnormal skin, normal hair, abnormal nails, normal sweat secretion and a normal tear secretion

* = Sweat secretion
# = Tear secretion

Logistic regression is a statistical technique, to predict or describe the dependence of a binary variable from a set of independent variables (Hosmer and Lemeshow, 1989). Logistic regression can be used for estimating the probability that a patient has oligodontia/I (considering this category arbitrarily as our response of interest), depending on the values of one or more covariables like symptoms of the skin, hair and so on.

Logistic regression and chi-square tests were used to examine possible differences between the control group and the group of patients with oligodontia/I.

**Table 7.4** *Patterns of congenitally missing teeth.*

| | |
|---|---|
| Prem1, Prem2 | 14; 15; 24; 25; 34; 35; 44; 45 |
| Can1, Can2 | 13; 23; 33; 43 |
| Incm1, Incm2 | 11; 21; 16; 26 |
| Celabo1, Celabo2 | 31; 32; 41; 42; 12; 22 |
| Cebo1, Cebo2 | 31; 41; 11; 12; 21; 22 |
| Mola1, Mola2 | 17; 27; 37; 47 |
| Lat1, Lat2 | 12; 22; 32; 42 |
| Cen1, Cen2 | 11; 21; 31; 41 |
| Mol1, Mol2 | 16; 26; 36; 46 |
| Prem1, Can1 etc.: | patients in which all teeth mentioned are congenitally missing |
| Prem2, Can2 etc.: | patients in which all teeth mentioned are present |

## 7.3 Results

### 7.3.1 Comparison between oligodontia/I - oligodontia/S and a control group

The major oral and extra-oral symptoms which occurred in patients with oligodontia and the control group are summarized in the Tables 7.5 and 7.6. The dental symptoms were described in the Chapters 5 and 6.

The main oral symptoms are listed in Table 7.5. No significant differences (Chi-square tests) at a significance level of 0.01 were found concerning oral symptoms studied between patients with oligodontia/I and patients with oligodontia/S. In Table 7.6 the main extra-oral symptoms are given, which occurred in the three different groups. The main extra-oral symptoms found in patients with oligodontia/S were a dry skin, sparse hair, lessened or increased eyebrows, abnormal nails and a reduced sweat and tear secretion. Patients with oligodontia/S also more often showed an abnormal shape of the ears, nose and forehead than patients with oligodontia/I. However, those differences were not significant.

In comparing the occurrence of oral and extra-oral symptoms of patients with oligodontia/I with the control group, the skin, enamel defects, the interrelationship between maxilla and mandible, the interocclusal distance and the physiognomy en face were significantly different (Chi-square tests; $P < 0.01$; Tables 7.5-7.6).

**Table 7.5** *Frequencies of oral symptoms occurring in patients with oligodontia and the control group.*

| | Oligodontia/S | | Oligodontia/I | | Oligodontia/I-S | | Control group | |
|---|---|---|---|---|---|---|---|---|
| Oral symptoms | N = 48 | | N = 89 | | N = 30 | | N = 135 | |
| | N | % | N | % | N | % | N | % |
| Enamel defects[##] | | | | | | | | |
| - yes | 6 | 12.5 | 9 | 10.1 | 3 | 10.0 | 5 | 3.7 |
| - no | 40 | 83.3 | 66 | 74.2 | 23 | 76.7 | 129 | 95.6 |
| - missing value | 2 | 4.2 | 14 | 15.7 | 14 | 13.3 | 1 | 0.7 |
| Frenula labialis[*,#] | | | | | | | | |
| - both normal | 21 | 43.8 | 49 | 55.1 | 16 | 53.3 | 87 | 64.4 |
| - attached sup[1]. | 26 | 54.2 | 34 | 38.2 | 13 | 43.3 | 40 | 29.6 |
| - attached inf[2]. | 1 | 2.1 | 1 | 1.1 | | | 1 | 0.7 |
| - both attached | | | 3 | 3.4 | 1 | 3.3 | 4 | 3.0 |
| - missing value | | | 2 | 2.2 | | | | |
| Clefting[*,#] | | | | | | | | |
| - present | 4 | 8.3 | 2 | 2.2 | 1 | 3.3 | | |
| - absent | 44 | 91.7 | 85 | 95.5 | 29 | 96.7 | 135 | 100 |
| - missing value | | | 2 | 2.2 | | | | |
| Relation max[3].- mand[4;*,##] | | | | | | | | |
| - normal | 28 | 58.3 | 56 | 62.9 | 21 | 70.0 | 117 | 86.7 |
| - abnormal | 20 | 41.7 | 31 | 34.9 | 9 | 30.0 | 17 | 12.6 |
| - missing value | 9 | | 2 | 2.2 | | | 1 | 0.7 |
| Interocclusal distance[*,##] | | | | | | | | |
| - normal | 28 | 58.3 | 63 | 70.8 | 22 | 73.3 | 119 | 88.1 |
| - more than 4 mm | 19 | 39.6 | 23 | 25.8 | 8 | 26.7 | 6 | 4.1 |
| - missing value | 1 | 2.1 | 3 | 3.4 | | | 10 | 7.9 |
| Physiognomy en face[*,##] | | | | | | | | |
| - normal | 23 | 47.9 | 46 | 51.7 | 12 | 40.0 | 113 | 83.7 |
| - deep set plica mentalis | 25 | 52.1 | 39 | 43.8 | 17 | 56.7 | 19 | 14.1 |
| - missing | | | 4 | 4.5 | 1 | 3.3 | 3 | 2.2 |

**Legend Tables 7.5 and 7.6:**

1 = superior 2 = inferior
3 = maxilla 4 = mandibula

In the comparison of the groups all abnormalities were put together in one category. Tested was normal against abnormal, Chi-square tests were used.

* = Comparison between patients with oligodontia/S and oligodontia/I, non significant at a significance level of 0.01.
** = Comparison between patients with oligodontia/S and oligodontia/I, significant ($P < 0.01$).
\# = Comparison between the control group and patients with oligodontia/I, non significant at a significance level of 0.01.
\#\# = Comparison between control group and patients with oligodontia/I, significant ($P < 0.01$).

**Table 7.6** *Frequencies of extra-oral symptoms occurring in patients with oligodontia and the control group.*

| | Oligodontia/S | | Oligodontia/I | | Oligodontia/I-S | | Control group | |
|---|---|---|---|---|---|---|---|---|
| | N = 48 | | N = 89 | | N = 30 | | N = 135 | |
| | N | % | N | % | N | % | N | % |
| Skin**,## | | | | | | | | |
| - normal | 13 | 27.1 | 64 | 71.9 | 18 | 60.0 | 123 | 91.1 |
| - dry | 35 | 72.9 | 25 | 28.1 | 12 | 40.0 | 12 | 8.9 |
| Hair**,# | | | | | | | | |
| - normal | 18 | 37.5 | 83 | 93.3 | 21 | 70.0 | 132 | 97.8 |
| - sparse/thick | 30 | 62.5 | 6 | 6.7 | 9 | 30.0 | 3 | 2.2 |
| Eyebrows**,# | | | | | | | | |
| - normal | 21 | 43.8 | 82 | 92.1 | 26 | 86.7 | 128 | 94.8 |
| - lessened/increased | 27 | 56.3 | 5 | 5.6 | 4 | 13.3 | 6 | 4.5 |
| - missing value | | | 2 | 2.2 | | | 1 | 0.7 |
| Nails**,# | | | | | | | | |
| - normal | 19 | 39.6 | 78 | 87.6 | 14 | 46.7 | 124 | 91.9 |
| - abnormal | 29 | 61.4 | 11 | 13.4 | 16 | 53.3 | 11 | 8.1 |
| Sweat secretion**,# | | | | | | | | |
| - normal | 22 | 45.8 | 71 | 79.8 | 24 | 80.0 | 119 | 88.1 |
| - lessened | 20 | 41.7 | 8 | 9.0 | 2 | 6.7 | 16 | 11.9 |
| - increased | 6 | 12.5 | 10 | 11.2 | 3 | 10.0 | | |
| - missing value | | | | | 1 | 3.3 | | |
| Tear secretion**,# | | | | | | | | |
| - normal | 37 | 77.1 | 89 | 100 | 22 | 73.3 | 131 | 97.0 |
| - lessened | 6 | 12.5 | | | 1 | 20.0 | 3 | 2.2 |
| - increased | 4 | 8.3 | | | 6 | 3.3 | 1 | 0.7 |
| - missing value | 1 | 2.1 | | | 1 | 3.3 | | |
| Nose shape*,# | | | | | | | | |
| - normal | 39 | 81.3 | 84 | 94.4 | 28 | 93.3 | 126 | 93.3 |
| - abnormal | 9 | 18.8 | 5 | 5.6 | 2 | 6.7 | 9 | 6.7 |
| Location of ears*,# | | | | | | | | |
| - normal | 44 | 91.7 | 86 | 96.7 | 27 | 90.0 | 133 | 98.5 |
| - low-set ears | 2 | 4.2 | 2 | 2.2 | 3 | 10.0 | 2 | 1.5 |
| - missing value | 2 | 4.2 | 1 | 1.1 | | | | |
| Shape of ears*,# | | | | | | | | |
| - normal | 37 | 77.1 | 81 | 91.0 | 26 | 86.7 | 118 | 87.4 |
| - abnormal | 11 | 22.9 | 8 | 9.0 | 4 | 13.3 | 13 | 9.6 |
| - missing value | | | | | | | 4 | 3.0 |
| Forehead*,# | | | | | | | | |
| - normal | 43 | 89.6 | 85 | 95.5 | 28 | 93.3 | 134 | 99.3 |
| - frontal bossing | 5 | 10.4 | 4 | 4.5 | 2 | 6.7 | 1 | 0.7 |

No differences were found both between patients with oligodontia/I and oligodontia/S and between oligodontia/I and the control group concerning shape and size of the tongue and craniomandibular dysfunctions.

Comparing the occurrence of combinations of extra-oral symptoms in patients with oligodontia/I and the control group, a significant higher frequency of combinations of one or more ectodermal abnormalities was found for patients with oligodontia/I ($X^2 = 8.2$; $P < 0.001$; Table 7.7). However, no significant difference was found in the occurrence of combinations of two or more ectodermal abnormalities between the two groups ($X^2 = 3.3$; $P = 0.1$; Table 7.7).

Using logistic regression no model could be built to discriminate between patients with oligodontia/I and the control group using the combinations of extra-oral symptoms as independent variables.

**Table 7.7** *Distributions of combinations of extra-oral symptoms in patients with oligodontia/I and the control group.*

| Patients with oligodontia/I | | | Control group | | |
|---|---|---|---|---|---|
| Combinations of extra-oral symptoms | | | Combinations of extra-oral symptoms | | |
| | Number of abnormalities (Table 7.3) | | | Number of abnormalities (Table 7.3) | |
| | | Frequency of occurrence | | | Frequency of occurrence |
| C2 | (4) | 1 | C7 | (3) | 1 |
| C6 | (3) | 2 | C8 | (2) | 1 |
| C12 | (2) | 4 | C12 | (2) | 2 |
| C14 | (2) | 2 | C14 | (2) | 3 |
| C16 | (1) | 15 | C16 | (1) | 4 |
| C22 | (2) | 1 | C23 | (2) | 1 |
| C24 | (1) | 1 | C28 | (1) | 9 |
| C26 | (2) | 1 | C30 | (1) | 13 |
| C28 | (1) | 2 | C31 | (1) | 1 |
| C30 | (1) | 9 | C32 | (0) | 98 |
| C32 | (0) | 32 | | | |
| Total number of patients | | 84 | Total number of patients | | 133 |

C1-C32 correspond with C1-C32 as presented in Table 7.3

$X^2$ (one or more ectodermal abnormalities) = 8.2 ($P = 0.001$)
$X^2$ (two or more ectodermal abnormalities) = 3.3 ($0.05 < P < 0.1$)

The results of the correspondence analysis (CA) are shown in Figure 7.1. Figure 7.1 shows the relationship among the three groups of patients and specific combinations of extra-oral symptoms. The combinations of extra-oral symptoms with one or two ectodermal abnormalities (C16, C26, C14) are grouped around the patients with oligodontia/I, whereas most of the combinations with 3 or more ectodermal abnormalities (C1, C2, C3 C5, C9, C10, C11, C19) are grouped around the patients with oligodontia/S. The combination with no ectodermal abnormalities (C32) is closest to the control group. In this plot, the first dimension describes 81.5% of the inertia, whereas the second dimension describes 18.5% of the inertia.

**Figure 7.1** *Correspondence analysis plot displaying the relation between combinations of extra-oral symptoms and the three groups (patients with oligodontia/I; patients with oligodontia/S and the control group) studied.*

The plot should be interpreted in the following manner: in this plot the first dimension (horizontal axis) which describes 81.5% of the inertia (a measurement of the chi-square) is more important than the second dimension which describes 18.5% of the inertia. Therefore, the points in this plot should be projected on the horizontal axis, to evaluate the closeness of the points. Points which appear close together are assumed to be associated. The distance from the origin determines the degree of association.

O/S = patients with oligodontia/S; O/I = patients with oligodontia/I; con = control group
1-32 are in correspondence with C1-C32, for an explanation of C1 - C32 see Table 7.3.
* = origin

### 7.3.2 Associations between congenitally missing teeth and extra-oral symptoms

The relationship between the total number of congenitally missing teeth and specific combinations of extra-oral symptoms is shown in Figure 7.2. Most points, representing the number of missing teeth and combinations of extra-oral symptoms, appear close together, around the origin. An exception was seen of C1 (all 5 symptoms abnormal), which appeared close to a number of 27-28 missing teeth,

C4 (abnormal skin, hair and nails) and C10 (normal hair and tear secretion) appeared close to the group with a total number of 24-26 missing teeth. Finally, C12 (abnormal skin and nails) appeared close to 21-23 congenitally missing teeth. In this plot the first dimension describes 31.8% of the inertia and the second dimension 19.7%.

**Figure 7.2** *Correspondence analysis plot displaying the relation between the total number of congenitally missing teeth and combinations of extra-oral symptoms.*

The plot should be interpreted in the same manner as in Figure 7.1. In this plot, the first dimension (horizontal axis) describes 31.8% of the inertia (a measurement of the chi-square) and is more important than the second dimension which describes 19.7% of the inertia. However, the difference between the first and second dimension is not so large as in Figure 7.1. Therefore, the points should be projected on both axes, to evaluate the closeness of the points.

6-8, 9-11 etc. represents the total number of congenitally missing teeth
1-32 are in correspondence with C1-C32, for an explanation of C1-C32 see Table 7.3.
* = origin; A = C6; C9; C19; 18-20; B = C14; C2; 21-26; C = C11; 15-17; D = C28; C32; E = C16; 6-8; F = C25; C30; 22-24; G = C24; C15; C23

Differences between patients with for example all canines present (can2) and patients with all canines absent (can1; Table 7.4), were analyzed by means of the frequencies of combinations of extra-oral symptoms (Table 7.3) occurring in patients with different patterns of congenitally missing teeth. When comparing the patterns of congenitally missing teeth which represents the absence of teeth (can1, prem1 etc.) with the patterns of congenitally missing teeth which represents the presence of teeth (can2, prem2 etc) the patterns representing the absence of teeth showed significantly higher frequencies of combinations of extra-oral symptoms with two or more ectodermal abnormalities (Chi-square tests; $P < 0.01$).

No significant differences, using a test for the difference between proportions, were found between the different extra-oral symptoms when comparing the proportions of patterns of congenitally missing teeth which occurred in patients whom showed the different extra-oral symptoms. Patients with an abnormal skin showed the same distribution of the patterns of congenitally missing teeth as the patients with for example abnormal nails.

Significant differences were found between proportions of abnormal extra-oral symptoms and the congenitally missing of the upper central incisors compared with abnormal extra-oral symptoms and the congenitally missing of other teeth. The proportion of persons with an abnormal skin, hair, nails or sweat secretion was significantly higher in the case of congenitally missing upper central incisors than in the case of the congenital missing of other teeth.

## 7.4 Discussion

In literature, patients with oligodontia/I are discriminated from patients with oligodontia/S, using the criteria of extra-oral symptoms (Oligodontia/S) or absence of extra-oral symptoms (Oligodontia/I; Jorgenson, 1980). Graber (1978) suggested that there might exist microforms of ectodermal dysplasia, just as there exist microforms of hypodontia. During examination of the patients in the present study it appeared that some patients with oligodontia/I did show minor symptoms of ectodermal dysplasia. To the author's knowledge, there are no other studies in which the patients with oligodontia/I are compared with a control group concerning oral and extra-oral symptoms, with exception of the study of Tso et al. (1985). These authors studied the number of sweat pores in patients with hypodontia compared with a control group.

In the present study, significant differences in oral symptoms were found between patients with oligodontia/I and the control group. Due to the number of missing teeth it can be expected that patients with oligodontia/I more often show a deep set plica mentalis, an increased interocclusal distance and an abnormal interrelationship between maxilla and mandible. Those results are in agreement with findings presented in literature (Hobkirk and Brook, 1980).

A comparison of the frequencies of extra-oral symptoms between patients with oligodontia/I and the control group revealed only one significant difference. Patients with oligodontia/I more often had a dry skin than the control group. This could be due to a lower number of sweat pores in patients with oligodontia/I, as described in the study of Tso et al. (1985). These authors found a lower mean sweat pore count in patients with hypodontia compared with a control group. Sweat secretion was not quantified in the present study.

From examination of the frequencies of combinations of extra-oral symptoms occurring in both groups it could be concluded that the control group and the patients with oligodontia/I were almost the same concerning their composition of specific combinations of extra-oral symptoms (Table 7.7). The difference between the two groups was significant evaluating the number of persons with one or more ectodermal abnormalities compared with the persons with no ectodermal abnormalities in both groups, this is due to the significant difference between the

skin (C16), as described above.

Using logistic regression, no satisfactory model could be built to discriminate between the patients with oligodontia/I and the control group, using the combinations of extra-oral symptoms, confirming that the two groups are almost the same in their composition of combinations of extra-oral symptoms.

The preceding results are illustrated in Figure 7.1. In the plot the association between combinations of extra-oral symptoms and the three groups is shown. Groups of patients and combinations of ectodermal symptoms which appear close together are assumed to be associated. The points should be projected on the horizontal axis to evaluate the closeness of the points, since the first axis describes the largest amount of the inertia (81.5%). The distance from the origin determines the degree of association between a group of patients and a combination of extra-oral symptoms.

As is shown in Figure 7.1, patients with oligodontia/I show a low degree of association with combinations of extra-oral symptoms with one or two ectodermal abnormalities (C16, C26, C14) since the patients with oligodontia/I are located near the origin when projecting on the first dimension. On the contrary, patients with oligodontia/S show a relatively strong degree of association with combinations of 3 or more ectodermal abnormalities (C1, C2, C3 C5, C9, C10, C11, C19). Not all patients with oligodontia/S do show all symptoms of ectodermal dysplasia. Therefore, also combinations of one or two ectodermal symptoms (C6, C8, C15, C22, C24) are grouped around these patients. The association of the control group with the combination of absence of ectodermal abnormalities (C32) is somewhat stronger than the association of the patients with oligodontia/I, but still low compared with that of the patients with oligodontia/S. In Figure 7.1, patients with oligodontia/I and the control group appear near to each other in the plot, also indicating that the groups hardly differ in their composition of specific combinations of extra-oral symptoms.

In literature, patterns of congenitally missing teeth are described in certain syndromes (Jorgenson, 1980). The group of patients with oligodontia/S mainly consisted of patients with ectodermal dysplasia (both hypohidrotic and hyperhidrotic). Some patients with oligodontia/I also showed symptoms of ectodermal dysplasia. Therefore, in this study for statistical analysis only a sufficient number of patients with symptoms of ectodermal dysplasia was available (Table 7.2). Possible associations between patterns of congenitally missing teeth and the main extra-oral symptoms which occurred in patients with ectodermal dysplasia were examined. The main ectodermal symptoms found in patients with oligodontia were a dry skin, sparse hair, lessened or increased eyebrows, abnormal nails and abnormal sweat and tear secretion.

The patterns of congenitally missing teeth (Table 7.4) and combinations of extra-oral symptoms (Table 7.3) evaluated in this study were chosen and based on an extensive search for information concerning possible combinations from the literature (Jorgenson, 1980; Hall, 1983; Tso et al., 1985; Childers and Wright, 1986; Gorlin et al., 1990). It is possible that combinations which were difficult accessible have been overlooked.

From evaluation of the relation between specific patterns of congenitally missing teeth and combinations of extra-oral symptoms it could be concluded that the patients in whom the different types of teeth were absent (Table 7.4) showed different

combinations of extra-oral symptoms compared to the patients in whom those different types of teeth were present. In the group of patients in whom the different types of teeth were present, significantly lower frequencies of combinations with two or more ectodermal abnormalities were found compared to the group of patients in whom the same types of teeth were absent. This would suggest that there must be significant differences in the occurrence of ectodermal symptoms between patients with oligodontia (absence of teeth) and the control group (presence of teeth). However, no significant differences were found between the patients with oligodontia/I and the control group. This contradiction is due to the considerable number of patients with oligodontia/S that is present in the evaluation of the association between patterns of congenitally missing teeth and the combinations of extra-oral symptoms. The patients with the combinations of 3 or more ectodermal abnormalities are patients with ectodermal dysplasia (oligodontia/S). In those patients the mean number of missing teeth is higher than in patients with oligodontia/I, even the most stable teeth (central upper incisors and first molars) are frequently missing in those patients (Tso et al., 1985; Chapter 4).

No definite associations were found between main extra-oral symptoms such as an abnormal skin, hair and nails and patterns of congenitally missing teeth, in both patients with oligodontia/I and oligodontia/S. No associations were found between any of the extra-oral symptoms examined and congenitally missing teeth, with the exception the upper central incisor. In the case of the congenital missing of the upper central incisors a significantly higher proportion of abnormalities was found than in case of the congenital missing of other teeth.

Concerning the relationship between the total number of missing teeth and combinations of extra-oral symptoms, a relatively strong association was found between the combinations with 3 or more ectodermal abnormalities (C1, C10) with a number of missing teeth larger than 24 (Fig. 7.2).

## 7.5 Conclusions

In conclusion, the results of the present study indicate that normal persons also show minor symptoms of ectodermal dysplasia such as abnormal nails or fine hair. The control group and the patients with oligodontia/I only differ significantly in the frequency of an abnormal skin. Therefore, it can be concluded from the present study that it is correct to appoint a group of patients with oligodontia/I. However, one should take into account that in the present study the patients were only clinically examined, no laboratory aids or other techniques were used to determine the presence or absence of symptoms. In case of a patient with congenitally missing teeth, the general practitioner should always perform a careful examination searching for minor symptoms of ectodermal dysplasia to rule out the possibility of oligodontia/S.

Furthermore, it can be concluded from the present study that there are no clear associations between individual or combinations of extra-oral symptoms of ectodermal dysplasia (i.e. dry skin, abnormal nails etc.) and individual or patterns of congenitally missing teeth. The associations found between patterns of congenitally missing teeth, the total number of missing teeth and extra-oral symptoms confirm

statistically what could be concluded from literature using common sense. Patients with oligodontia/S are the patients with the ectodermal abnormalities and the highest number of missing teeth. Therefore, it is logical to assume that absence of teeth is associated with combinations of two or more ectodermal abnormalities. Even the most stable teeth are missing in these patients, which resulted in the association of the upper central incisor and abnormalities. For the general practitioner this means that if the most stable teeth are missing or, if the number of missing teeth is large, one should examine the patient carefully for symptoms of ectodermal dysplasia.
The general practitioner should be aware of the possibility of congenitally missing teeth if patients show features of ectodermal dysplasia.

# Chapter 8
# Environmental and genetic factors contributing to oligodontia[1]

## 8.1 Introduction

It is known that oligodontia can be the result of either environmental or genetic factors or a combination of the two. The exact etiology and pathogenesis of both forms however, is unclear.

As described in Chapter 2, the main environmental factors that can cause oligodontia are: local influences on the jaws (Lee et al., 1989); constitutional diseases (Grahnen, 1956) and trophoneurotic and endocrine disturbances, which interfere with jaw development and mineralization (Werther and Rothenberg, 1939; Sarnat et al., 1988).

According to literature, genetic factors are the most important etiological factors of oligodontia. Many authors consider oligodontia to be the result of a single gene (Grahnen, 1956; Philip and Caurdy, 1985). They suggest a Mendelian pattern of inheritance. An autosomal dominant trait with incomplete penetrance and variable expressivity is often suggested as an explanation (Grahnen, 1956; Philip, 1985; Ranta, 1985). Rosenberg (1982) suggested an X-linked transmission. All statements were based on family studies.

Other authors consider oligodontia to be determined by a multifactorial trait. Suarez and Spence (1974), Chosack et al. (1975), Bailit (1975) and Brook (1984) suggested a polygenic model: the anomaly is the result of a summation of genetic factors. Usually a polygenic inheritance is seen in continuous traits such as stature and intelligence (Chosack et al., 1975) However, some discontinuous traits such as cleft lip and palate also show a polygenic mode of inheritance (Carter, 1969). The absence of teeth is also a discontinuous variable. Chosack et al. (1975) assumed that hypodontia was the result of a polygenic inheritance with a threshold effect. Those individuals below the biological threshold remain unaffected while those above this threshold are affected. Bailit (1975) assumes that hypodontia is a quasicontinuous trait. The absence of teeth tends to arise near the extremes of a continuous variable such as tooth size. Brook (1984) proposes a similar model combining polygenic and environmental factors.

It is known that the teeth of patients with oligodontia show reduced mesiodistal dimensions as compared to a control group (Baum and Cohen, 1971; Brook, 1984; Chapter 5). In establishing the mode of inheritance, it is important to know if these size reductions of teeth also occur in relatives of the patients with oligodontia.

The aim of the present study was i) to evaluate environmental factors that could have contributed to oligodontia; ii) to establish a reduction in tooth size in relatives of patients with oligodontia and iii) to make a contribution to the knowledge of the possible mode of inheritance of patients with isolated oligodontia.

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[1] This chapter is an edited version of the manuscript entitled: "A contribution to the etiology of oligodontia" (authors: Schalk-van der Weide Y; Beemer FA; Bosman F), which has been submitted to Journal of Dental Research (August, 1992).

## 8.2 Materials and methods

The study material comprised 166 patients with oligodontia (83 males and 83 females). Mean age was 24 years, with age range being 6 to 54 years. Orthopantomograms were available in order to confirm the congenital missing of six or more teeth excluding the third molars. Only patients who gave informed consent for the use of the data were included in the study. The group consisted of 47 patients with oligodontia/S, 89 patients with oligodontia/I and 30 patients in which neither oligodontia/I or oligodontia/S could be confirmed. Only patients with oligodontia/I were included in the study to determine the mode of inheritance.

Upon examining the patients, a specially-designed form was used, as described in paragraph 3.3.1. All patients as well as their relatives were examined by one of the authors (YSW).

To gather information from the patients relatives, a questionnaire was given to the patients following the clinical examination, as described in paragraph 3.3.2.

The patients were asked to obtain the information on their relatives directly from the relatives themselves. In addition, a short questionnaire was made up for the relatives. Questions were asked concerning congenitally missing teeth and ectodermal symptoms and permission was asked to gather and use additional information from the family dentist.

Dentists were asked to determine if there were any congenitally missing teeth and to point out size reductions, such as conical and peg-shaped teeth, of the teeth present. Finally, the dentist was asked to make a set of dental impressions. For as far as this was possible, this examination was combined with the person's routine visit to their dentist.

Casts of 59 relatives (33 females and 26 males) of patients with oligodontia were collected. Five relatives were relatives of patients with oligodontia/S. The mesiodistal dimensions of the teeth of the relatives were compared with the standard mesiodistal dimensions of the teeth as given by Moyers et al. (1976) according to the procedure described in Chapter 5.

The genetic part of the study comprised 50 patients (22 females and 28 males) about whom sufficient information was available to construct a pedigree. Information, considered as reliable was registered, including anamnestic data. Statistical segregation analyses were carried out according to the methods described by Emery (1986). The following methods, assuming multiple incomplete ascertainment, were used: the probands method and the modified "singles" method (Emery, 1986).

## 8.3 Results

### 8.3.1 Environmental factors

The main anamnestic data concerning health of mother and child are summarized in Table 8.1. In the majority of the patients the anomaly was familial.

In general, the pregnancies were uneventful. The events recorded were, among other things, fever, pneumonia, toxoplasmosis and diabetes mellitus.

A small percentage of the mothers used drugs shortly before or during the pregnancy. Antibiotics and anti-epileptics were mentioned amongst these.

Only two mothers had a radiography (stomach and feet) during the pregnancy. No other traumatic injuries were recorded. Only a minority of the women continued smoking or drinking during pregnancy, and one women had been smoking hash.

Several diseases occurring during the first three years of life were observed in 34 % of the children. Flue with high fever, typhoid fever, viral meningitis and gastrointestinal disorders were mentioned. Approximately twenty-five percent of the young patients were given prescription drugs during the first three years of life. Prednison, various antibiotics, anti-epileptics, thiazinamium and others were mentioned as being used.

**Table 8.1** *Clinical history of patients with oligodontia.*

| Type of oligodontia | | O/S | O/I | O/I-S |
|---|---|---|---|---|
| Number of patients in each group | | 47 | 89 | 30 |
| | Familial | 81 % | 67 % | 87 % |
| Mothers: | | | | |
| Age at the start of pregnancy | 20 - 29 years<br>30 - 34 years<br>35 > | 51 %<br>17 %<br>4 % | 43 %<br>22 %<br>8 % | 53 %<br>30 %<br>7 % |
| Duration | Premature<br>Normal<br>Late | 2 %<br>85 %<br>9 % | 4 %<br>87 %<br>4 % | 3 %<br>83 %<br>10 % |
| Birth | Problems<br>Normal | 4 %<br>93 % | 4 %<br>92 % | 10 %<br>87 % |
| Drugs | Used<br>Not used | 13 %<br>87 % | 6 %<br>91 % | 3 %<br>93 % |
| Trauma | No<br>Yes | 100 %<br>0 % | 98 %<br>0 % | 93 %<br>3 % |
| Smoking/ drinking | No<br>Yes | 91 %<br>9 % | 96 %<br>2 % | 90 %<br>7 % |
| Children: | | | | |
| Illnesses during first 3 years | Yes<br>No | 34 %<br>66 % | 34 %<br>65 % | 27 %<br>70 % |
| Drugs | Used<br>Not used | 26 %<br>72 % | 25 %<br>75 % | 13 %<br>83 % |
| Trauma | No<br>Yes | 96 %<br>4 % | 93 %<br>6 % | 97 %<br>0 % |

Note: the total in all columns should be a 100%. However, in some cases the clinical history was not complete (missing values). Therefore, there are some columns with a percentage lower than a 100%.

### 8.3.2 Mesiodistal dimensions of the teeth of relatives of patients with oligodontia

The results of the measurements of mesiodistal dimensions of the teeth of first and second degree relatives of patients with oligodontia are presented in the Tables 8.2 and 8.3. The mesiodistal dimensions of the teeth in the control group are described in Chapter 5 (Tables 5.1 and 5.2).

The mesiodistal dimensions of the teeth of those relatives with a full permanent dentition showed significant reductions in comparison to the control group. For both male and female relatives, the lower central and lateral incisor and the upper central

incisor were significantly reduced ($P < 0.01$). In contrast, the lower first molar was larger in relatives of the patients with oligodontia, in comparison to the control group. In females as well, the upper lateral incisor was significantly reduced in comparison to the control group ($P < 0.01$).

Measurements taken of the mesiodistal tooth dimension in those relatives with congenitally missing teeth revealed significant reductions in comparison to the control group. In both male and female relatives, the upper and lower central incisor and the lower canine were significantly reduced ($P < 0.01$). In addition male relatives showed a significant reduction in the upper lateral incisor, canine and second premolar. In female relatives, the lower lateral incisor was also significantly reduced ($P < 0.01$). The number of congenitally missing teeth in the relatives varied from 1 to 17, with a mean of 4 congenitally missing teeth.

**Table 8.2** *Mesiodistal dimensions of the teeth of female relatives of patients with oligodontia.*

| Tooth | N1 | X1 | SD | Xc | N2 | X2 | SD |
|---|---|---|---|---|---|---|---|
| Maxilla | | | | | | | |
| I1 | 19 | 7.9 | 0.9** | 8.7 | 9 | 7.9 | 0.7** |
| I2 | 18 | 6.3 | 0.4** | 6.8 | 9 | 6.3 | 0.5 |
| C | 21 | 7.6 | 0.5 | 7.5 | 8 | 7.2 | 0.7 |
| P1 | 16 | 6.8 | 0.6 | 6.6 | 5 | 6.4 | 0.5 |
| P2 | 15 | 6.7 | 0.5 | 6.5 | 3 | 6.6 | 0.8 |
| M1 | 14 | 10.2 | 0.6 | 10.2 | 6 | 10.0 | 1.5 |
| Mandible | | | | | | | |
| I1 | 23 | 5.2 | 0.4** | 5.5 | 9 | 5.0 | 0.6** |
| I2 | 23 | 5.7 | 0.4* | 5.9 | 8 | 5.5 | 0.5** |
| C | 21 | 6.5 | 0.4 | 6.6 | 9 | 6.1 | 0.4** |
| P1 | 20 | 6.7 | 0.5 | 6.8 | 10 | 6.6 | 0.6 |
| P2 | 15 | 7.1 | 0.5 | 7.1 | 5 | 6.9 | 0.7 |
| M1 | 13 | 10.8 | 0.5** | 10.3 | 4 | 10.7 | 0.8 |

**Legend Tables 8.2 and 8.3:**

X1; X2 = mean mesiodistal dimension (in mm) of the teeth of females
X3; X4 = mean mesiodistal dimension (in mm) of the teeth of males
Xc = mean mesiodistal dimension (in mm) of the teeth of the control group
N1; N3 = number of relatives with a full permanent dentition
N2; N4 = number of relatives with congenitally missing teeth
SD = standard deviation ; ** = $P < 0.001$; * $P < 0.01$

X1 and X2 were compared with the control group in Chapter 5, Table 5.1 (page 36).
X3 and X4 were compared with the control group in Chapter 5, Table 5.2 (page 37).
N and SD of the control group are presented in the Tables 5.1 and 5.2.

### 8.3.3 Genetic analysis

The genetic part of the study comprised the families of probands with isolated oligodontia. One hundred forty-three new cases of oligodontia were revealed in these 50 families. The pedigrees of all families are shown in Appendix 2. At first sight the pedigrees were divided in autosomal dominant inheritance (AD), autosomal recessive inheritance (AR), sporadic cases and co-dominance. However, for segregation analysis all pedigrees were put together.

The mode of inheritance of oligodontia was compatible with AD inheritance at first sight in 38 families (Pedigrees 1-38). In those 38 families 129 new cases (62 female and 67 male) with oligodontia were found. In 6 of the families with AD inheritance, X-linked dominant (XD) inheritance appeared to be a possible theoretical alternative (Pedigrees 28-33). Theoretically, AR inheritance was also possible in five families (Pedigrees 34-38).

**Table 8.3** *Mesiodistal dimensions of the teeth of male relatives of patients with oligodontia.*

| Tooth | N3 | X3 | SD | Xc | N4 | X4 | SD |
|---|---|---|---|---|---|---|---|
| Maxilla | | | | | | | |
| I1 | 14 | 8.4 | 0.5** | 8.9 | 9 | 8.0 | 0.5** |
| I2 | 15 | 6.6 | 0.5 | 6.9 | 4 | 6.2 | 0.8* |
| C | 14 | 7.8 | 0.4 | 8.0 | 8 | 7.6 | 0.3* |
| P1 | 12 | 7.0 | 0.5 | 6.8 | 9 | 6.7 | 0.6 |
| P2 | 11 | 6.8 | 0.4 | 6.7 | 6 | 6.2 | 0.5* |
| M1 | 10 | 10.7 | 0.5 | 10.6 | 5 | 10.0 | 0.4 |
| Mandible | | | | | | | |
| I1 | 16 | 5.1 | 0.3** | 5.5 | 6 | 5.0 | 0.3** |
| I2 | 16 | 5.8 | 0.4* | 6.0 | 6 | 5.7 | 0.4 |
| C | 16 | 6.8 | 0.3 | 7.0 | 8 | 6.6 | 0.4* |
| P1 | 15 | 7.0 | 0.5 | 6.9 | 9 | 6.6 | 0.4 |
| P2 | 15 | 7.1 | 0.4 | 7.2 | 4 | 7.0 | 0.5 |
| M1 | 10 | 11.1 | 0.3** | 10.7 | 6 | 10.6 | 0.5 |

The mode of inheritance of oligodontia in four families was at first sight compatible with AR inheritance (Pedigrees 39-42). Theoretically, the mode of inheritance in one family was also compatible with X-linked recessive (XR) inheritance (Pedigree 42). In those families, four additional patients (2 females, 2 males) were diagnosed.

There were six sporadic cases, i.e. the proband was the only person known in each family (Pedigrees 43-48). Theoretically these sporadic cases were also compatible with AD spontaneous mutation or AR inheritance. In two families, the mode of inheritance was compatible with co-dominance (Pedigrees 49-50).

Using the proband method a p of 0.38 was found. Using the modified "singles" method p was $0.35 \pm 0.045$.

The prevalence of congenitally missing teeth among first degree relatives of the

patients with oligodontia is given in Table 8.4. The total number of affected first-degree relatives was 34.5 %. In the family study, more females than males were affected. However, the difference was not significant ($X^2=0.41$, $P \approx 0.5$). The number of affected first-degree relatives from female probands was higher than that of male probands. Again the difference was not significant ($X^2=1.46$, $0.25 < P < 0.1$).

No significant differences were found in the frequencies of affected relatives of probands with various degrees of oligodontia (Table 8.5). However, an increased risk was shown for relatives when more than one member of the family was affected (Table 8.6).

**Table 8.4** *Analysis of 50 families of probands with isolated oligodontia.*

| | Family study | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Siblings | | | | Parents | | | |
| | male | | female | | male | | female | |
| | aff[1] | un[2] | aff | un | aff | un | aff | un |
| Male probands | 20 | 21 | 8 | 23 | 3 | 25 | 9 | 19 |
| Female probands | 5 | 12 | 10 | 10 | 7 | 15 | 10 | 12 |

**Legend Table 8.4**:
1 = affected; 2 = unaffected

Total number affected first-degree relatives = 72 (34.5%), which results in a penetrance of 69%

**Table 8.5** *The occurrence of congenitally missing teeth in first-degree relatives by number of missing teeth of the proband.*

| Number of missing teeth | First-degree relatives | |
|---|---|---|
| | Hypodontia | No hypodontia |
| 6-10 | 30 (29.7 %) | 71 |
| > 11 | 35 (35.0 %) | 65 |

$X^2$(6-10/ > 11)=0.64 ($0.25 < P < 0.5$)

Percentage first-degree relatives in other classifications of congenitally missing teeth of the proband: 6-12 (30.9%); > 13 (31.8%); 6-15 (31.3%); > 16 (31.7%)

*Clinical analysis pedigrees*

The mean number of congenitally missing teeth in the male probands was 12.44 ± 4.6. In the male relatives, a mean number of 4.75 ± 6.7, range 1-28 was found. In female probands, a mean number of 10.34 ± 3.3 was found. A mean number of 5.1 ± 5.96 congenitally missing teeth was found in the female relatives, range 1-28.

In some probands and relatives, minor symptoms of ectodermal dysplasia were found. A total number of 143 new cases with oligodontia were found; 11 of these showed reduced teeth only.

**Table 8.6** *Number of affected siblings when more than one family member is affected.*

| | Affected siblings | Unaffected siblings |
|---|---|---|
| Unaffected parents (21 families) | 13 | 58 |
| At least one affected parent (29 families) | 26 | 43 |

$X^2 = 6.49$ ( $0.01 < P < 0.025$)

## 8.4 Discussion

It is known that oligodontia can be the result of environmental and/or genetic factors (Chapter 2). In this part of the study, therefore attention was paid also to the occurrence of possible environmental factors. No obvious causative environmental factors were found in this study. Environmental factors which could possibly have contributed to oligodontia, such as high fever and extraction of deciduous teeth, were observed mainly in patients with other affected family members. In those familial cases, it is unlikely that oligodontia was the result of environmental factors as mentioned.

In first and second-degree relatives with a full permanent dentition, results of the measurements of mesiodistal dimensions of the teeth revealed significant differences between the relatives of the probands with oligodontia and the control group, for both males and females (Tables 8.2 - 8.3). In an earlier study (Chapter 5) it appeared that nearly all mesiodistal dimensions of the teeth of patients with oligodontia were significantly reduced in comparison to a control group. The results of the present study confirm those of other studies (Baum and Cohen, 1971; Brook, 1984): reduction in tooth size must be seen as being associated with oligodontia. To the author's knowledge, no studies have been performed where the mesiodistal dimensions of the teeth were taken in relatives of patients with oligodontia. Measurements of the mesiodistal and labiolingual dimensions of teeth have been performed of relatives of patients with ectodermal dysplasia (Airenne, 1981). Significant reductions in tooth size were described in these relatives. The results of the present study show that measurements of the mesiodistal dimensions of the teeth of relatives are important and could be necessary in revealing the correct mode of inheritance. In the genetic study, therefore, a person was also marked as being affected if he or she showed reductions in tooth size.

In Chapter 7, symptoms occurring in patients with isolated oligodontia were compared with those of a control group. It was concluded that minor symptoms of ectodermal dysplasia could be found in normal persons as well. Although minor ectodermal symptoms did occur in probands and relatives, this information was not included in the pedigrees.

It was very difficult to obtain information from older generations. In a large number of families, it was not known whether any members of the family had congenitally missing teeth. In general practice, there is no registration of congenitally missing teeth in patients. Nevertheless, patients with large numbers of congenitally missing teeth are often known as such, since these are exceptions. The recognition of patients with one or two congenitally missing teeth, however, is more difficult. This made it difficult to obtain retrospective information from the dentists concerning patients with congenitally

missing teeth. It is possible that in the families presented here the real number of affected relatives is underestimated.

The value of p found using the proband method and modified "singles" method were lower than could be expected in case of AD inheritance, 0.38 and 0.35 $\pm$ 0.045 respectively. Using the modified "singles" method p ranges from 0.26 to 0.44 (p $\pm$ 2 SD). Therefore, AR inheritance can not be completely excluded. However, AD inheritance is more likely especially if one takes into account the reduced penetrance of 69% as found in the present study (Table 8.4). The results are in agreement with the results of earlier studies (Grahnen, 1956; Philip and Caurdy, 1985; Ranta, 1985).

Many authors consider oligodontia to be a multifactorial trait (Brook, 1984; Chosack et al., 1975). It is known that differentiating between an AD inheritance and a multifactorial trait poses some difficulties. Therefore, the data were also analyzed for compatibility with multifactorial inheritance.

The criteria for a multifactorial trait as described by Brook (1984) and Chosack et al. (1975) are the following: First, the proportion of affected relatives should be greater than the population frequency, but less than the frequency expected by single gene inheritance. Secondly, the risk varies from family to family. Thirdly, relatives run an increased risk of being affected if more than one member of the family is affected. Finally, the relatives of the less frequently affected sex are more likely to have affected relatives than relatives of the more frequently affected sex.

In the present study, the proportion of affected relatives was 34.5% (Table 8.5). In the Netherlands, no prevalence of congenitally missing teeth is known. Nevertheless, as described in Chapter 4, a prevalence of the congenital missing of six or more teeth of 0.08% was found. Therefore, it could be concluded that the rate of occurrence of congenitally missing teeth in relatives of probands with oligodontia was significantly higher than that of the population. The 34.5 % found was lower than could be expected when assuming AD inheritance. In our study ,the risk varied slightly from family to family but did not reach the level of significance (Table 8.6). However, there was a significantly increased risk if more than one family member was affected (Table 8.7). In the present study, of first-degree relatives slightly more females than males were affected. However, the difference was not significant. In contrast to what could be expected from the multifactorial trait criteria, the relatives of the females showed a higher risk of being affected. However, the difference, once again was not significant. The results of the present study are only partly compatible with multifactorial inheritance.

When comparing the results of Brook's study (1984) with our own, Brook's results concerning the risk of relatives to be affected in case of various number of missing teeth in the probands attracts attention. Brook (1984) founds that the risk of being affected was significantly different between relatives of probands with six or more congenitally missing teeth and those with less than six congenitally missing teeth. The same was found in an earlier study by Grahnen (1986). In the present study, only probands with six or more congenitally missing teeth were included. The striking observation made was that the risk of being affected did not differ significantly between groups of probands with differing numbers of congenitally missing teeth.

## 8.5 Conclusions

It can be concluded from the present study, that no obvious causative environmental factors could be discriminated. Factors that could possibly have contributed to oligodontia were high fever, pemphigus, extraction of the deciduous teeth, viral meningitis and the use of prednison and various antibiotics.

The results of the present study show that measurements of the mesiodistal dimensions of the teeth in relatives are important and might be necessary for revealing the correct mode of inheritance. After all, size reductions of teeth were also found in family members with a full permanent dentition.

The mode of inheritance was in agreement with an AD mode of inheritance with a reduced penetrance. A reduced penetrance of 69% was found.

Apparently, the discrimination between groups of patients with many congenitally missing teeth (six or more) and few congenitally missing teeth (less than six) seems to be not only a theoretical discrimination but also a biological one. Differences were found concerning mode of inheritance in probands with more than six congenitally missing teeth (present study) as compared to the complete group of probands with more than six and less than six congenitally missing teeth (Brook, 1984).

# Chapter 9
# Crown-size profile and asymmetry patterns[1]

## 9.1 Introduction

As described in the Chapters 2 and 8, the exact etiology and pathogenesis of oligodontia is still unclear. An autosomal dominant mode of inheritance is suggested as an explanation (Grahnen, 1956; Rosenberg, 1982; Ranta, 1985). Other authors consider oligodontia to be determined by a multifactorial trait (Suarez and Spence, 1974; Chosack et al., 1975; Brook, 1984). Such a model combines genetic and environmental influences. The genetic components of a multifactorial system may be widely distributed throughout the genome. According to Brook (1984), the presence of dental anomalies in syndromes due to certain chromosomal anomalies could indicate the site of some of the genes influencing tooth number and size.

The genetic background of tooth size has been the subject of several studies. Because of their short period of formation and constant size after mineralization, tooth crowns are well-suited to genetic studies. Much of individual's pre and postnatal development can be appraised by examining the teeth (Werner and Harris, 1989). It is known that tooth size is influenced by the sex chromosomes. Both X- and Y-chromosomes apparently carry genes affecting phenotypic tooth size (Alvesalo, 1971). The relative influence of the X- and Y-chromosome is different. Genes located on the X-chromosome appear to regulate the thickness of the enamel and appear to influence on the development of the roots. Genes located on the Y-chromosome appear to regulate mitotic cell activity (Varrela, 1991).

Patterns of tooth size reductions have been studied in many syndromes; this is done by measuring the mesiodistal and labiolingual dimensions of the teeth. These crown-size profile patterns can contribute to the knowledge of i) the etiology of a syndrome or ii) the mechanism of the anomalies of the teeth. When the etiology of a certain syndrome is known, an indication can be given concerning the mechanism of the tooth anomalies. On the other hand, if the etiology of the syndrome is unknown, a contribution to the knowledge of the etiology of that syndrome can be made using the information from the dental anomalies.

Syndromes in which crown-size profile patterns have been reported are: Down syndrome, 45,X/46,XX females, cleft lip and palate and female carriers of X-linked ectodermal dysplasia (Airenne, 1981; Townsend, 1983; Varrela et al., 1988; Werner and Harris, 1989). The crown-size profile patterns can also have diagnostic value (Garn and Lewis, 1970).

So far, no studies have been performed in which the labiolingual dimensions of the teeth of patients with oligodontia were measured.

Several studies have evaluated left-right asymmetries of the teeth in order to determine developmental instability, or reduced buffering capacity, in patients with several syndromes (Sofaer, 1979; Townsend et al., 1986; Werner and Harris, 1989).

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[1] This chapter is an edited version of the manuscript entitled: "Crown-size profile and asymmetry patterns: a contribution to the etiology of oligodontia" (authors: Schalk-van der Weide Y; Steen WHA; Beemer FA; Bosman F), which has been submitted to the Archives of Oral Biology (June, 1992).

The aims of the present study were to compare i) the crown-size profile patterns and ii) left-right asymmetry patterns of patients with oligodontia with these same patterns in patients with other syndromes in order to contribute to the knowledge of the etiology of oligodontia.

## 9.2 Materials and methods

The study comprised 82 patients (41 males and 41 females) with oligodontia. A detailed description of the group is given in Chapter 5.

Patients with oligodontia were compared with patients with the following syndromes: Down syndrome (Townsend, 1983), 45,X/46,XX females (Varrela et al., 1988), cleft lip and palate (Werner and Harris, 1989) and carrier females of X-linked ectodermal dysplasia (Airenne, 1981). In a percentage of the patients with Down syndrome, the diagnosis trisomy 21 was established by cytogenic tests. The other patients with Down syndrome were diagnosed on a phenotypic basis. The karyotype of all 45,X/46,XX females was confirmed by cytogenic tests of skin fibroblasts. In the cleft lip and cleft palate group, patients with other systemic anomalies were excluded from the study even as the isolated cleft palate patients. In a study made up of X-linked ectodermal dysplasia, only female relatives suspected to be carriers, proved to have a sufficient quantity of measurable teeth.

The measurements of the mesiodistal dimensions are described in Chapter 5. However, now a comparison is made with the mesiodistal dimensions of the teeth of the control group Townsend (1983). The labiolingual dimensions of the teeth were measured on casts and compared with the tooth dimensions of a control group as given by Townsend (1983). The maximum labiolingual dimensions of a tooth were only measured if the tooth was fully erupted and no dental restorations had been made. The labiolingual dimension recorded was the maximal distance between labial and lingual surfaces in the plane perpendicular to that in which the mesiodistal dimension was measured (Moorrees et al., 1957). Measurements were made with a digital measuring instrument. The accuracy of this instrument was to 0.01 mm.

Experimental errors were analyzed by a replicability trial in which the labiolingual dimensions of teeth selected at random were measured twice. A Student's t-test was used to determine if there were significant differences between the first and second measurements. A mean difference of 0.016 mm was found for the labiolingual measurements and 0.042 mm for the mesiodistal dimensions (Chapter 5). The differences between the first and second measurements were not significant.

The Kolmogorov-Smirnov test was used to test the normality of the measurements, after which an F-test was performed and either a Student's t-test or a Welch's test were performed to determine significance differences between the patients with oligodontia and the control group (Pearson and Hartley, 1966; Harnett, 1982).

When possible, the asymmetry patterns were also compared. Sufficient information of the asymmetry patterns was available from patients with Down syndrome, 45,XO (Turner syndrome) and cleft lip and palate patients (Townsend et al., 1986; Werner and Harris, 1990). In those two studies, different methods were used to assess the asymmetry patterns. The same methods were used to be able to compare the patients with oligodontia with these studies.

Werner and Harris (1989) used the following formula to calculate left-right asymmetry in cleft lip and palate patients: |L-R|/(L+R/2). Townsend et al. (1986) used the variance (V) of (R-L)/(R+L) as a measurement of asymmetry in patients with Down syndrome and 45,XO females. In both formulas R and L represent corresponding measurements on right and left sides respectively.

## 9.3 Results

The mesiodistal dimensions of the teeth of patients with oligodontia are presented in the Tables 5.1 and 5.2. The mesiodistal dimensions of the second molars are presented in Table 9.1. All mesiodistal dimensions of teeth of patients with oligodontia were significantly reduced compared to the mesiodistal dimensions of the teeth of the control group.

**Table 9.1** *Mesiodistal dimensions of the second molars.*

| | N1 | X1 | SD | Xc1 | N2 | X2 | SD | Xc2 |
|---|---|---|---|---|---|---|---|---|
| Maxilla | | | | | | | | |
| M2 | 11 | 9.6* | 0.5 | 10.0 | 12 | 9.2*** | 0.9 | 10.3 |
| Mandible | | | | | | | | |
| M2 | 8 | 9.5*** | 0.4 | 10.5 | 4 | 10.2* | 0.9 | 11.0 |

**Legend Table 9.1:**

X1 = mean mesiodistal dimension (in mm) of the teeth of females
X2 = mean mesiodistal dimension (in mm) of the teeth of males
Xc1 = mean mesiodistal dimension (in mm) of the teeth of females of the control group
Xc2 = mean mesiodistal dimension (in mm) of the teeth of males of the control group
N1,2 = number of teeth measured
* = $P < 0.01$; *** = $P < 0.001$

The labiolingual dimensions of the teeth of patients with oligodontia are presented in the Tables 9.2 and 9.3. Compared with the control group, the labiolingual dimensions of the following teeth were not significantly reduced: a) the lower second molar in females and b) the lower central incisor in males.

In the Tables 9.4 and 9.5, the proportional differences of the mean mesiodistal and labiolingual dimension are given for the various syndromes. For patients with oligodontia, the largest proportional differences in mesiodistal dimensions were found in males with the upper lateral incisor and the lower second premolar (17-20%) and in females with the upper central and lower lateral incisor (11-13%). In both sexes, the canines were the less-affected teeth. For the labiolingual dimensions, the largest proportional differences, were found with the first and second premolars (12-23%), in both sexes.

**Table 9.2** *Labiolingual dimensions of maxillary and mandibular teeth of females with oligodontia and the control group.*

| | N1 | X1 | SD | N2 | X2 | SD |
|---|---|---|---|---|---|---|
| Maxilla | | | | | | |
| I1 | 31 | 6.4*** | 0.6 | 57 | 7.1 | 0.5 |
| I2 | 11 | 5.9* | 0.5 | 55 | 6.3 | 0.5 |
| C | 18 | 7.4*** | 0.5 | 51 | 8.1 | 0.4 |
| P1 | 14 | 7.5*** | 1.0 | 53 | 9.2 | 0.5 |
| P2 | 2 | 7.8** | 1.7 | 56 | 9.2 | 0.6 |
| M1 | 36 | 10.3*** | 0.9 | 92 | 11.4 | 0.5 |
| M2 | 9 | 10.2*** | 0.6 | 44 | 11.4 | 0.7 |
| Mandible | | | | | | |
| I1 | 12 | 5.6** | 0.3 | 65 | 5.9 | 0.4 |
| I2 | 23 | 5.7*** | 0.5 | 63 | 6.2 | 0.4 |
| C | 20 | 6.6*** | 0.6 | 54 | 7.4 | 0.5 |
| P1 | 27 | 6.8*** | 0.6 | 55 | 7.8 | 0.5 |
| P2 | 6 | 7.1*** | 0.5 | 56 | 8.4 | 0.6 |
| M1 | 32 | 9.9*** | 0.6 | 87 | 10.5 | 0.5 |
| M2 | 9 | 9.9# | 0.7 | 44 | 10.3 | 0.6 |

**Legend Tables 9.2 and 9.3:**
N1; N3 = sample size of patients with oligodontia
N2: N4 = sample size of the control group
X1; X2 = mean labiolingual dimension (in mm) of the teeth of females
X3; X4 = mean labiolingual dimension (in mm) of the teeth of males
SD = standard deviation
*** = $P < 0.001$; ** = $P < 0.01$; * = $p < 0.05$; # = non-significant

Patients with oligodontia showed severe reductions in tooth size of both early and late-developing teeth, whereas patients with Down syndrome showed a reduction in tooth size in later-developing teeth and the females with 45,X/46,XX showed a reduction in early-developing teeth (Tables 9.4-9.5). Carrier females of X-linked hypohidrotic ectodermal dysplasia also showed a severe reduction in both early and late-developing teeth (Tables 9.4-9.5). In patients with cleft lip and palate, both early and late-developing teeth were affected (Table 9.4).

The asymmetry patterns of patients with oligodontia and cleft lip and palate, using the method of Werner and Harris (1990), are shown in Figure 9.1. The patterns were comparable. The asymmetry patterns of patients with Down syndrome, 45,X/46,XX and oligodontia, using V (variance of (R-L)/(R+L)) as a measurement of asymmetry, are shown in the Figures 9.2-9.3. In all groups of teeth, the more distal teeth were most severely affected.

**Table 9.3** *Labiolingual dimensions of maxillary and mandibular teeth of males with oligodontia and the control group.*

| | N3 | X3 | SD | N4 | X4 | SD |
|---|---|---|---|---|---|---|
| Maxilla | | | | | | |
| I1 | 32 | 6.5** | 0.8 | 69 | 7.3 | 0.5 |
| I2 | 5 | 5.9** | 0.7 | 59 | 6.5 | 0.5 |
| C | 11 | 7.6*** | 0.8 | 64 | 8.5 | 0.5 |
| P1 | 9 | 7.4*** | 0.7 | 58 | 9.4 | 0.5 |
| P2 | 8 | 7.4*** | 0.5 | 67 | 9.5 | 0.6 |
| M1 | 31 | 10.5*** | 1.0 | 83 | 11.7 | 0.5 |
| M2 | 10 | 10.7** | 1.1 | 58 | 11.8 | 0.7 |
| Mandible | | | | | | |
| I1 | 9 | 5.9# | 0.5 | 69 | 6.2 | 0.5 |
| I2 | 11 | 6.1* | 0.4 | 66 | 6.4 | 0.4 |
| C | 12 | 7.0** | 1.1 | 59 | 7.9 | 0.5 |
| P1 | 23 | 7.1*** | 0.7 | 55 | 8.2 | 0.5 |
| P2 | 5 | 6.8*** | 0.9 | 63 | 8.6 | 0.5 |
| M1 | 27 | 10.3*** | 0.7 | 80 | 10.8 | 0.5 |
| M2 | 4 | 9.7** | 1.4 | 57 | 10.7 | 0.6 |

**Figure 9.1** *Asymmetry patterns (|L-R|/(L+R/2)) of patients with oligodontia and cleft lip and palate according to the method of Werner and Harris (1989).*

**Table 9.4** *Proportional differences of the mean of the mesiodistal dimensions of maxillary and mandibular teeth of females and males with oligodontia, Down syndrome, 45,X/46,XX females, female carriers with X-linked ectodermal dysplasia and patients with cleft lip and palate.*

| | DOx% | DDx% | DXx% | DHx% | DOy% | DDy% | DCxy% |
|---|---|---|---|---|---|---|---|
| Maxilla | | | | | | | |
| I1 | 12.5*** | 8.3** | 6.9*** | 11.5*** | 12.7*** | 3.6*** | 7.9* |
| I2 | 10.4*** | 16.7** | 4.4* | 5.9 | 17.3*** | 14.3*** | 7.6* |
| C | 6.6*** | 14.3** | 1.3 | 12.9*** | 6*** | 14.3*** | 9.9* |
| P1 | 10.7*** | 8.5** | 4.3* | 11.4*** | 13.1*** | 10.1*** | 2.1 |
| P2 | 9.2* | 10.8** | 8.8*** | 11.8*** | 12.5*** | 10.1*** | 0.005* |
| M1 | 8.4*** | 5.9** | 6.9** | 7.8** | 9.8*** | 4.9*** | 0.008 |
| M2 | 4.2* | 17.1** | 3.1* | 5.2* | 10.9*** | 18.6*** | 6.9* |
| Mandible | | | | | | | |
| I1 | 5.9*** | 4.6** | 9.0*** | 9.0** | 7.9*** | 2.8* | 1.1 |
| I2 | 11.5*** | 10.7** | 6.7*** | 6.7* | 8.3*** | 8.3*** | 5.3* |
| C | 6.6*** | 10.7** | 1.5 | 4.5* | 4.5** | 10.7*** | 4.4* |
| P1 | 9.0*** | 9.2** | 2.9 | 5.7* | 8.9*** | 8.1*** | 3.2* |
| P2 | 9.0** | 8.3** | 4.2 | 7.1*** | 19.9*** | 9.4*** | 2.2* |
| M1 | 5.9*** | 5.3** | 7.3** | 8.2** | 9.8*** | 6.5*** | 3.2* |
| M2 | 9.7*** | 13.5** | 2.9* | 9.6** | 6.8* | 14.5*** | 2.9* |
| Mean | 8.5 | 10.3 | 5.5 | 8.4 | 10.6 | 9.7 | 4.1 |

**Legend Tables 9.4 and 9.5:**

D = $(X_{patients} - X_{control})/X_{control}$

DOx,y% = proportional difference of the mean of females (DOx%) and males (DOy%) with oligodontia

DDx,y% = proportional difference of the mean of females (DDx%) and males (DDy%) with Down syndrome

DXx% = proportional difference of the mean of 45,X/46,XX females

DHx% = proportional difference of the mean of heterozygote females with ectodermal dysplasia

DCxy% = proportional difference of the mean of males and females with cleft lip and/or cleft palate

*** = $P < 0.001$

** = $P < 0.01$

* = $P < 0.05$

**Table 9.5** *Proportional differences of the mean of the labiolingual dimensions of maxillary and mandibular teeth of females and males with oligodontia, Down syndrome, 45,X/46,XX females, female carriers with X-linked ectodermal dysplasia.*

| | DOx% | DDx% | DXx% | DHx% | DOy% | DDy% |
|---|---|---|---|---|---|---|
| Maxilla | | | | | | |
| I1 | 9.9*** | 11.7** | 4.1 | 8.2*** | 10.9** | 12.5** |
| I2 | 6.3* | 14.6* | 1.6 | 1.6 | 9.2** | 16.4** |
| C | 8.6*** | 19.5** | 0 | 9.8*** | 10.6*** | 20.5** |
| P1 | 18.5*** | 16.1** | 0 | 9.8** | 21.3*** | 17.2** |
| P2 | 15.2** | 18.3** | 0 | 9.7*** | 22.1*** | 19.5** |
| M1 | 9.6*** | 10.2** | 1.8 | 7.0** | 10.3*** | 10.9** |
| M2 | 10.5*** | 15.2** | 1.8 | 4.5 | 9.3** | 15.5** |
| Mandible | | | | | | |
| I1 | 5.1** | 11.8** | 0 | 8.3** | 4.8 | 14.6** |
| I2 | 8.1*** | 13.1** | 1.6 | 6.3* | 4.7* | 13.0** |
| C | 10.8*** | 14.3** | -1.3 | 12*** | 11.4** | 13.4** |
| P1 | 12.8*** | 14.8** | -1.3 | 6.4** | 13.4*** | 14.1** |
| P2 | 15.5*** | 14.7** | -2.4 | 8.3** | 20.9*** | 15.1** |
| M1 | 5.7*** | 7.0** | 5.6*** | 5.6** | 4.6*** | 8.2** |
| M2 | 3.9 | 13.2** | 2.9 | 2.9 | 9.3* | 14.9** |
| Mean | 10.0 | 13.9 | 1.02 | 7.2 | 11.6 | 14.7 |

**Figure 9.2** *Asymmetry patterns (V=(R-L)/(R+L)) in the maxilla of patients with oligodontia and patients with Down syndrome and Turner (45,XO) syndrome according to the method of Townsend et al. (1986).*

**Figure 9.3** *Asymmetry patterns (V=(R-L)/(R+L))* in the mandible of patients with oligodontia and patients with Down syndrome and Turner (45,XO) syndrome according to the method of Townsend et al. (1986).

## 9.4 Discussion

In a previous part of the study (Chapter 5), the mesiodistal dimensions of the teeth of patients with oligodontia were compared with those of a control group as given by Moyers et al (1976). The mesiodistal dimensions reported by Moyers et al. (1976) were comparable to the mesiodistal dimensions as reported by Townsend (1983) with exception of the second molar. The mesiodistal dimensions of the second molars as reported by Moyers et al. (1976) were smaller than those found in patients with oligodontia, in contrast to what could be expected. Since the second molar is important for the crown-size profile pattern in the present study, the mesiodistal dimensions of all teeth were compared with those as reported by Townsend (1983). All mesiodistal dimensions of the teeth of patients with oligodontia were significantly reduced when compared to the control group of Townsend (1983).

To the author's knowledge, no studies have been performed in which the labiolingual dimensions of the teeth of patients with oligodontia have been determined. However, from clinical inspections of the teeth of patients with oligodontia, a reduced labiolingual dimension can be expected. In the present study, a reduction of the labiolingual dimensions of nearly all teeth was found. A mean percentage of reduction of 11.6% and 10.0% for males and females respectively was found. The reduction in labiolingual dimensions was even more severe than the reduction in mesiodistal dimension of the teeth.

In developing teeth, the mesiodistal dimension is determined before the labiolingual dimension. The final crown morphology is the result of the interaction between the timing and rate of cellular proliferation in the developing tooth germ together with the

time of onset and spread of mineralization. The process of mineralization spreads down mesially and distally before moving cervically (Varrela et al., 1988).

The dental abnormalities in Down syndrome are thought to be due to a reduction in cellular mitotic activity resulting in growth retardation. According to this hypothesis, late-developing teeth or units (labiolingual dimensions) of these teeth should be more severely affected than early developing teeth. The results as presented by Townsend (1983) were in agreement with this hypothesis.

On the contrary, females with 45,X/46,XX showed a more severe reduction in the early-developing teeth. Moreover the labiolingual dimensions (late developing units of the teeth) showed only a minor reduction in size. The more severe reduction in mesiodistal dimension is due to the thinner enamel in those patients. It is known that the thickness of the enamel contributes more to mesiodistal dimensions than to labiolingual dimensions (Townsend et al., 1984).

In patients with oligodontia, both early and late-developing teeth were severely reduced. The female carriers of X-linked ectodermal dysplasia showed more or less the same crown-size profile pattern as the patients with oligodontia. The present study comprised 27 patients with oligodontia as part of ectodermal dysplasia. No statistical significant differences between these patients with ectodermal dysplasia and patients with isolated oligodontia could be found concerning tooth size. These patients, therefore, were included in the study.

From the cleft lip and palate patients, only sufficient information concerning the proportional differences of the mean mesiodistal dimension was available.

The crown-size profile patterns of the patients with oligodontia as presented in this study showed resemblance to the crown-size profile pattern of patients with cleft lip and palate as presented by Werner and Harris (1989). Both early and late-developing teeth were severely affected in those patients with cleft lip and palate as well (Tables 9.4 and 9.5).

In patients with cleft lip and palate, Down syndrome and 45,XO, asymmetries of the dental anomalies were reported (Sofaer, 1979; Werner and Harris, 1989; Harris and Hullings, 1990).

No differences were found between the left and right sides concerning the distribution of congenitally missing teeth, mesiodistal dimensions of the teeth and tooth formation in patients with oligodontia (Chapters 4-6). However, the fact that no differences were observed between left and right sides does not exclude the occurrence of asymmetries in these patients.

The methods used by Sofaer (1979) and Townsend et al. (1986), are statistically spoken, preferable. Unfortunately, the results as presented by Sofaer (1979) were insufficient for the purposes of comparing them to the present study. Werner and Harris (1989) used absolute values as a measurement of asymmetry, and standard deviation units to visualize the pattern profiles for proportionate asymmetry, although their data were not normally distributed. Since no other study was available for comparison purposes the same method was used in this study. However, one must bear in mind that, statistically, no conclusions can be drawn.

As is shown in Figures 9.1, 9.2 and 9.3, the teeth in the groups with the anomalies were more asymmetric than the teeth in the control group. In all groups, the more distal tooth, i.e. the lateral incisors, second premolars and second molar, tended to show greater asymmetry than the more mesial teeth. No statements can be made concerning

the significance of the differences in asymmetry between the control group and patients with oligodontia, Down syndrome, Turner syndrome and cleft lip and cleft palate. However, the occurrence of asymmetry in tooth development indicates a reduced buffering capacity, or developmental instability in these patients (Sofaer, 1979).

## 9.5 Conclusions

From this part of the study, the conclusion can be drawn that the size reduction of the teeth of patients with oligodontia appears to be due to other mechanisms than in Down syndrome and 45,X/46,XX females. The reason for this is that, in Down syndrome the late-developing teeth and in 45,X/46,XX females the early-developing teeth were most severely reduced, whereas in patients with oligodontia both early and late-developing teeth were severely reduced.

The resemblance of the crown-size profile pattern and the occurrence of asymmetry in patients with cleft lip and palate to oligodontia support the hypothesis that oligodontia and clefts are probably the result of the same etiological factor (Ranta, 1983). According to a later study, delayed tooth formation, advanced hypodontia and the clefts are likely to be the result of a prenatal insult interacting with a poorly buffered genotype (Ranta, 1984b). The genetic component in the multifactorial situation does not act directly to produce the malformation itself but indirectly through a reduction in buffering. Both cleft lip and palate and oligodontia are known as a multifactorial trait (Sofaer, 1979; Brook, 1984).

More research is needed to reveal the etiology of oligodontia. Crown-size profile patterns and asymmetry patterns of larger samples of patients and their relatives with oligodontia of both deciduous and permanent dentition could provide additional worthwhile information concerning etiology.

# Chapter 10
# Discussion and recommendations for further research

## 10.1 Discussion of the methods

In this study, three approaches have been used to gather the data on patients with oligodontia: i) clinically examining the patients, ii) questioning the patient, her/his parents and the dental practitioner and iii) measuring by means of dental casts and examining by means of orthopantomograms.

*Clinical examination*

During the clinical examination of the patients and controls, the author paid attention to the symptoms described earlier in literature (Chapter 2). Not all items in the clinical examination were quantitated. It would have been more accurate, for example, to count the number of sweat pores a patient had instead of questioning him/her about the sweat secretion. Criteria were formulated, as described in Chapter 3, and questions were asked or an examination was carried according to those criteria. The purpose of this was to assure that various symptoms were weighted as uniformly as possible through time. However, the experience, knowledge and insight gained by examining the patients might result in symptoms scored differently in the first and last patient examined. Facial features were also evaluated and scored by a clinical geneticist; results of both scores were compared and appeared to be similar.

*Questioning and questionnaires*

More than 500 patients were registered for the purpose of gathering information on oligodontia. However, this information proved insufficient for indicating the prevalence of oligodontia in the Netherlands. Unfortunately, no adequate registration exists of the number of individuals with congenitally missing teeth.

In this study, it was the intention to give at least an indication concerning the prevalence. Dental practitioners were asked to give the number of patients with oligodontia in their practice. It was assumed that the dental practitioner would remember these patients, as this anomaly is still highly unusual. Obviously, this will result in an underestimation of the number of patients. Firstly, the dentist will not remember all patients with oligodontia he or she has ever come in contact with. Secondly, patients younger than 9 or 10 years of age will not have been diagnosed as having congenitally missing teeth and, with patients older than 30 or 40, it is difficult to determine whether the cause of missing teeth is a congenital one. Therefore, in this study the prevalence of oligodontia is given of a population of patients within the age range of 15 to 44 years.

By questioning the patient and/or his parents, data were gathered concerning environmental factors and the occurrence of congenitally missing teeth in the family. Questioning the patient (or parents) according to a clear protocol minimizes the risk of forgetting items that are of potential importance to the study. In gathering data for constructing the pedigrees, the patient was asked to gather the information directly from family members. With the help of the patient and family dental practitioners, sufficient information of fifty families, was gathered for the present study

(Chapter 8). If more information would have been necessary family members could have been examined and questioned personally.

*Measuring by means of dental casts*

Dental casts were used to measure the size of the teeth and to study tooth morphology. The methods used to measure the mesiodistal and buccolingual dimensions of the teeth have been described in several studies. The measurements were taken with a digital measuring instrument with an accuracy to 0.01 mm, which was more than sufficient when taking into account the standard deviations (Tables 5.1 and 5.2; 9.2 and 9.3) and the limits of cast measurements.

Two limitations of cast measurements are the occurrence of plaster bubbles and the strength of the plaster. Locating the measuring instrument in such a way that the mesiodistal and buccolingual dimension can be adequately measured can be difficult because of plaster bubbles. A third aspect deserving attention is the dimensional changes that occur in plaster and impression materials. The setting expansion of plaster is different in different types of plaster, falling somewhere within the range of 0.05 - 0.3% (Craig et al., 1987). The setting expansion of plaster can be controlled by subjecting it to different manipulative conditions. Alginate impression material shows a tendency to contract between the time the impression is made and pouring of the plaster impression. These dimensional changes can be restricted to a minimum when the manufacturer's instructions are carefully followed.

When measuring dental casts, one should be aware of the possibility of dimensional inaccuracies.

*Measuring by means of orthopantomograms*

Finally, orthopantomograms (OPG's) were used to i) confirm the diagnosis of congenitally missing teeth and ii) to measure the length of the teeth and the occurrence of taurodontism.

As described in Chapter 6, OPG's are not ideal for measuring length due to radiographic magnification and distortion. However, in the present study these were the only radiographs available. It was considered ethically unacceptable to expose the patient to X-rays for the sole purpose of making a measurement of the length of teeth.

However, error-analysis, as described in Chapter 6 indicated that measuring by OPG made it possible to classify an individual as having a reduced length of teeth when length was 2.20 mm less than the mean length of the group concerned. The difference of 2.20 mm is within the range of the standard deviations of the length of teeth as found in both the control group and in patients with oligodontia. Therefore, measurements made by OPG were regarded as sufficiently accurate.

One of the other disadvantages to using this method was that a reduction in length of the roots or in height of the crown of teeth could not be determined. Anatomically, the crown is the part of the tooth covered by enamel, while the part covered by the cementum is the root (Lloyd DuBrull, 1980). On OPG's it is nearly impossible to determine the cementum-enamel junction of the tooth, which made it impossible to measure the length of the roots and the height of the crowns separately. Measuring the length of teeth indicates, at least, a reduction in length, without specifying whether the reduction was found in the crown or in the root. To

the author's knowledge, no studies have been performed so far for measuring the length of teeth, although some authors mention short roots in patients with congenitally missing teeth (Oliver et al., 1975; Ruprecht et al., 1986).

*Control groups*

In the present study, data of patients with oligodontia were compared with those of several control groups. The first control group consisted of data of mesiodistal dimensions of the teeth in normal individuals as reported by Moyers et al. (1976). A pilot study showed that the mesiodistal dimensions of the teeth in a Dutch group of normal individuals was comparable with the data provided by Moyers et al. (1976). However, in a later phase of the study, it appeared that data gathered by Moyers et al. (1976) concerning mesiodistal and buccolingual dimensions were slightly different from those reported by other authors. The mesiodistal and buccolingual dimensions of second molars and buccolingual dimensions of canines in Moyers et al. (1976), for example, were smaller than those dimensions given by other authors. Therefore, in Chapter 9 the data on mesiodistal and labiolingual dimensions of the teeth of normal individuals as reported by Townsend (1983) were used as a control.

Moyers et al. (1976) used a different method to measure the mesiodistal dimensions of the teeth then in the present study. Moyers et al. (1976) used the Optocom, designed and constructed at the University of Nijmegen, whereas in other studies measurements were performed by means of callipers. The Optocom is a microscope mounted over a table and movable in two dimensions. This instrument is useful when many points on dental casts must be stored. Especially with longitudinal data, the optocom has its advantages. The present study was not a longitudinal study and only mesiodistal and buccolingual dimensions were measured. Therefore, measuring with a measuring instrument was preferable to using the Optocom.

For studying dental age, children who participated in the Nijmegen Growth Study (Prahl-Andersen and Roede, 1979) were used as a control group. Another group of persons whose tooth formation was completed was necessary to study length of the teeth and taurodontism.

Finally, 135 persons with a full permanent dentition were clinically examined to gather information concerning the occurrence of oral and extra-oral symptoms in healthy persons. No radiographs were available on this group.

## 10.2 Discussion of the results

This study was begun to obtain information on several aspects of oligodontia, or congenitally missing teeth. Aspects studied were: i) symptomatology and ii) etiology. The aim of the study was to provide the dental practitioner with knowledge necessary to diagnose congenitally missing teeth and to inform the patient about the severity and nature of the disorder.

Congenitally missing teeth, or oligodontia, is not one of the main dental diseases in the Netherlands, as may be concluded from the prevalence described in Chapter 4. Generally the dental practitioner is confronted with two or three patients in his or her practice (Chapter 4). Therefore, diagnosing patients is difficult, because there is no "aha Erlebnis". Patients are often diagnosed after the age of 12 years when the

shedding of teeth is not on schedule. However, when attention is paid to signs and symptoms, patients can be diagnosed at an earlier stage.

From the present study, the conclusion can be made that in families with congenitally missing teeth all generations show symptoms of the dental anomaly, either in the form of congenitally missing teeth or in the form of a reduction in tooth size or tooth morphology (Chapters 5, 6 and 8). Therefore, if one of the parents show one of these signs, a dental practitioner should carefully examine the children clinically and radiographically in order to determine if they have a full permanent dentition. Extensive dental treatment can probably be avoided by doing so. Say, for example, that the orthopantomogram from one of the children of an affected parent reveals the congenital missing of four premolars. In this case, it might be possible to prevent bridges by premature extractions of the deciduous molars. The (pre)molars have the possibility to move forward, so the diastemas will be closed by the time the complete dentition is erupted. Furthermore, transplantations of unerupted mandibular molars have been described in literature (Hernandez and Cuestas-Carnero, 1988). This method can also be used in patients with oligodontia. However, the diagnosis must be made in an early stage of mandibular molar's development before root formation is more than two-thirds completed.

Of course if a child (adult) shows signs of a reduction in size of teeth or in tooth morphology (Chapters 5, 6 and 9), the dental practitioner should be aware of the possibility of congenitally missing teeth. Furthermore, these reductions in size and tooth morphology are of importance concerning dental therapy (Chapters 5 and 6).

The delay in tooth formation in this study was not so evident that it could be used as an important diagnostic criterion (Chapter 6). It is obvious, however, that in the event of a marked delay in eruption the presence or lack of a permanent successor must be determined. In the present study, patients with oligodontia showed a great individual variation in tooth formation. Also of importance are the consequences of a delay in tooth formation on the eruption times of the teeth. A delay in tooth formation does not per definition have to result in delayed eruption. The eruption pattern is important in the timing of orthodontic or prosthodontic treatment. The onset of therapy depends on teeth already erupted or approaching eruption.

Once the diagnosis "congenitally missing teeth" has been established, one should make a distinction between patients with oligodontia as part of a syndrome (Oligodontia/S) and isolated oligodontia (Oligodontia/I). As is presented in Chapters 4 and 7, there is a marked difference concerning the number of missing teeth and the extra-oral symptoms between the two groups of patients. The group of patients with oligodontia/S was missing significantly more teeth than the group of patients with oligodontia/I. Furthermore, patients with oligodontia/S, generally patients with signs of ectodermal dysplasia in this study, often have dry skin, abnormal nails, reduced or increased sweat secretion, etc. Although patients with oligodontia/I showed minor symptoms of ectodermal dysplasia one could conclude from the present study that it was correct to select a group of patients with oligodontia/I. However, one must bear in mind that in the present study no laboratory aids or other techniques were used to determine the presence or absence of symptoms (Chapter 7).

For the patient and/or his parents, the distinction between oligodontia/I and /S is rather important. Particularly if genetic counselling is desired. As is stated in Chapter 7, the recurrence risk in patients with oligodontia/S can be quite different

from that of the isolated type. In addition, the number and severity of the symptoms is - per definition - higher.

As described in literature, some syndromes show certain patterns of congenitally missing teeth, which can contribute to an early diagnosis. In this study, no direct associations were found between ectodermal symptoms and patterns of congenitally missing teeth in the patients with oligodontia/S (Chapter 7). One could conclude from the present study, however, that the dental practitioner should pay attention to the occurrence of ectodermal dysplasia in patients missing the most stable teeth (central incisors, first molars; Chapters 4 and 7).

To enable the general practitioner to make a quick distinction between patients with oligodontia/I and oligodontia/S, logistic regression as described in Chapter 6 and 7 was used to create a scheme with the most distinguishing symptoms.
The logistic regression model can be written as:

Probability (oligodontia/I) = $1/\ 1+e^{-z}$ (1)
where z is the linear combination:
$z=\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \ldots\ldots + \beta_p x_p$ (2)

where $\beta_0$ and $\beta_p$ are coefficients estimated from the data and $x_1$ thru $x_p$ are independent variables, such as skin, nails and hair. For prediction purposes one may say that linear combinations of $x_1$ thru $x_p$ which give rise to a probability of less than 0.5 discriminate between patients with oligodontia/I and oligodontia/S.

The results of the logistic regression concerning differentiation between patients with oligodontia/I and oligodontia/S are summarized in Table 10.1. Various models were constructed and evaluated using different methods and different combinations of symptoms. The model with the fewest misclassifications - e.g. patients with oligodontia/I were classified as oligodontia/S and vice versa - is presented in Table 10.1. According to this model (model 1), a patient can be classified as oligodontia/I with a specificity and sensitivity of 88.2%. An extra model was constructed leaving out the number of missing teeth. When the number of missing teeth is unknown, in young patients, for example, the specificity and sensitivity are still 82.4% and 79.4% respectively. In Table 10.1 it is also shown how the model should be used with new patients. The specificity and sensitivity of 88.2%, or 82.4 and 79.4% respectively with young patients gives the general practitioner a reliable indication as to whether the patient has oligodontia as part of a syndrome or isolated oligodontia.

In the present study, another attempt was been made to lift a corner of the veil concerning the etiology of oligodontia. It may be obvious now that oligodontia is not an isolated phenomenon but rather a complex of dental anomalies (Chapters 5-9).

In Chapter 8, it was shown that the pedigrees as constructed came closest to an autosomal dominant mode of inheritance with a reduced penetrance. The results of the comparisons of the crown-size profile patterns (Chapter 9) however, showed a resemblance between oligodontia and cleft lip and palate. As can be determined from literature, cleft lip and palate is usually caused by a multifactorial trait. The resemblance of the two groups could be an indication for multifactorial inheritance in oligodontia also. Literature has shown that it is often difficult to distinguish between an autosomal dominant mode of inheritance and a multifactorial trait, since both show more or less the same characteristics. Therefore, the results of Chapter 8 and 9

are not per definition contradictory. As stated in Chapter 9, more research is needed in order to reveal the exact pathogenesis of oligodontia.

**Table 10.1** *Logistic regression models concerning differentiation between patients with oligodontia/I and oligodontia/S.*

| | Model 1 | Model 2 | |
|---|---|---|---|
| Variables | ß | ß | |
| Hair by eyebrows* | 2.7 | 2.4 | ß1 |
| nails by eyebrows* | 3.2 | 2.7 | ß2 |
| hair* | -2.2 | -1.8 | ß3 |
| eyebrows* | -6.0 | -5.6 | ß4 |
| nails* | -4.4 | -4.8 | ß5 |
| tear secretion* | -6.6 | -6.4 | ß6 |
| number of missing teeth# | -2.6 | | ß7 |
| constant | 4.4 | 4.0 | |
| | | | |
| Selected group | | | |
| Specificity | 92.6 | 96.3 | |
| Sensitivity | 89.8 | 89.8 | |
| | | | |
| Unselected group | | | |
| Specificity | 88.2 | 82.4 | |
| Sensitivity | 88.2 | 79.4 | |

Values variables: *: 0 = normal; 1 = abnormal
#: 0 = less than 20 congenitally missing teeth
1 = more than 20 congenitally missing teeth

Example
Patient with normal nails and abnormal hair, tear secretion, eyebrows and less than 20 missing teeth

$P\ (\text{oligodontia/I}) = 1/1 + e^{-z}$

z = constant + ß1x(hair by eyebrows) + ß2x(nails by eyebrows) + ß3x(hair) + ß4x(eyebrows) + ß5x(nails) + ß6x(tear secretion) + ß7x(number of missing teeth)

$z = 4.4 + 2.7x(1x1) + 3.2x(0x1) - 2.2x(1) - 6.0x(1) - 4.4x(0) - 6.6x(1) - 2.6x(0)$
$= -7.7$

$P(\text{oligodontia/I}) = 1/1+e^{(-7.7)} = 4.5\ 10^{-4}$
Based on this estimate, which was less than 0.5, we would classify the patient as likely to have oligodontia/S.

## 10.3 Oligodontia or congenitally missing teeth?

Much can be said and has been said concerning the terminology used to describe congenitally missing teeth. In the present study, a working definition was used in which oligodontia was defined as the congenital missing of six or more teeth, excluding the third molars. This definition was chosen for several reasons, as described in Chapter 1. Firstly, these patients often have aesthetic and functional disturbances. Secondly, this definition holds with the definition as given by several other authors and, thirdly, it limits the group of patients.

The use of the term oligodontia or hypodontia is of secondary consideration as long as the terms used are defined clearly and unequivocally.

Research of this topic would be considerably less complicated if the terms used by authors were the same; as it stands, hypodontia and oligodontia are used, as well as many others (Chapter 2, Table 2.1).

From the results of the present study, it must be concluded that it is important to distinguish between congenitally missing teeth as part of a syndrome and as an isolated anomaly (Chapters 4 and 7). This distinction has not been made in every study. This aspect of congenitally missing teeth should not be underestimated.

Furthermore, from the family studies, as presented in Chapter 9, one can conclude that reduction in size of teeth can also occur in family members with a full permanent dentition. This indicates that this reduction in size of the teeth is a minimal expression of congenitally missing teeth.

It has been suggested that the term oligodontia should be reserved for congenitally missing teeth as part of a syndrome. However, there are also known syndromes with only one or two congenitally missing teeth (Appendix 1).

Many possibilities exist for defining and using terms to describe congenitally missing teeth (Chapter 2, Table 2.1). Three propositions will be discussed here.

Firstly, the option exists of using only one of the several terms used to describe the congenital missing of teeth, hypodontia for example. In doing so, however, one is hardly aware of the number of missing teeth or the severity of the disorder unless this is specifically mentioned.

Secondly, it is possible to reserve terms for the isolated type of congenitally missing teeth and congenitally missing teeth as part of a syndrome. Hypodontia could be used when discussing congenitally missing teeth of the isolated type and oligodontia for congenitally missing teeth as part of a syndrome. This makes the distinction between "isolated" and "as part of a syndrome" quite clear. However, the number of missing teeth still must be mentioned before one knows more about the severity of the disorder.

Finally, one can use both hypodontia and oligodontia for both the isolated type and the syndrome-related type. A distinction between isolated and syndrome-related variants of congenitally missing teeth can be made by using the terms used in this study, with the /I and /S extensions. Using these terms, the number of missing teeth and the severity of the disorder is known. In addition, these definitions take into account the possible difference in risk factor for being affected between family members with probands having six or more missing teeth and families with probands having less than six missing teeth (as described in Chapter 8).

Taking into account the results of the present study and the terms used and defined

in literature, the following definitions are proposed for use in future research:

| | |
|---|---|
| ***Hypodontia/I:*** | *the congenital missing of less than six teeth, excluding the third molars.* |
| ***Hypodontia/S:*** | *the congenital missing of less than six teeth, excluding the third molars, as part of a syndrome.* |
| ***Oligodontia/I:*** | *the congenital missing of six or more teeth, excluding the third molars.* |
| ***Oligodontia/S:*** | *the congenital missing of six or more teeth, excluding the third molars, as part of a syndrome.* |
| ***Anodontia/I:*** | *the congenital missing of all deciduous and/or permanent teeth.* |
| ***Anodontia/S:*** | *the congenital missing of all deciduous and/or permanent teeth, as part of a syndrome.* |

When not discussing one of the groups in particular, the use of the term congenitally missing teeth is appropriate.

When examining the mode of inheritance, size and form of teeth should be taken into account, as well as the congenital missing of third molars. In fact, these are all expressions of congenitally missing teeth.

## 10.4 Recommendations for further research

The subjects of interest for future research can be divided in subjects concerning further diagnostic aids and subjects concerning dental therapy.

*Diagnostic aids*

From the results of the present study (Chapter 7), one can conclude that it was correct to select a group of patients with isolated oligodontia. However, this was concluded using the results of clinical examinations. No laboratory aids were used to evaluate, for example, the structure of hair, nails etc. It is quite possible that the clinically abnormal hair or nails of the control group has another structure than the clinically abnormal hair or nails of the patients with oligodontia/I. Evaluation of symptoms should be performed using laboratory aids and other techniques necessary to reveal the differences rather than by clinical observations alone.

In order to reveal the pathogenesis of oligodontia, it could be of importance to confirm whether selecting a group of patients with oligodontia/I is truly justified. If no isolated oligodontia exists, then the congenital missing of teeth is always part of a complex of anomalies. This has consequences for the pathogenesis.

Clinical observations, as presented in this and other studies, will not lead to a better understanding of the etiology and pathogenesis of oligodontia. More knowledge of etiology and pathogenesis can probably be gained by studying the composition of the blood of patients with oligodontia/I and oligodontia/S.

Furthermore, studies on the DNA-level will reveal more about etiology and pathogenesis.

*Dental therapy*

Concerning dental therapy many fields remain open to research. Presently in most centres, the choice of dental therapy is ground on individual experiences and available material. One striking observation made was that every Department of Oral-Maxillofacial surgery, Prosthodontics and Special Dental Care visited had a "favourite" form of dental therapy used more than others. There were centres in which mainly crowns and bridges were used to restore the dentition. In other centres restoration of the dentition was mainly achieved by the use of partial prosthesis and overdentures. The deciduous molars often stay under the occlusal level of permanent teeth. In one of the centres, occlusal facings were used to restore deciduous teeth to the occlusal level of permanent teeth. Implants are not yet commonly used in patients with oligodontia. Although there are centres in which replacement of congenitally missing teeth had been done with dental implants, the indications still have to be investigated.

In literature, no straightforward criteria are provided for choosing dental therapy or for deciding at which age dental therapy should begun. There are too many items influencing indication, such as number of missing teeth, which teeth are missing and form and size of teeth. This makes establishing general criteria for dental therapy difficult. However, it is worthwhile to assess the effectiveness of dental therapy over the years. Evaluating the cause of failures and successes will enable the practitioner to establish an indication based not only on his/her own experiences but on those of others and scientific experiences as well.

Further research is particularly necessary with regard to the preservation of deciduous teeth. The deciduous teeth are very important in regard to preventing the resorption of the alveolar process. In patients with congenitally missing teeth, an underdevelopment of the alveolar process is often found. Literature on the subject has shown that the development of the alveolar process is partly due to the presence of teeth. Deciduous teeth, therefore, can be important instruments in preserving the bone of the alveolar process.

Examining these patients with oligodontia showed that deciduous teeth can be loaded with prosthetic constructions and still have a respectable lifetime. So far, no research has been performed to evaluate the possibilities of preserving deciduous teeth and the long-term influence on the alveolar process.

The preservation of deciduous teeth not only improves conditions for overdentures or partial prosthesis but can also improves conditions for dental implants on a later age. Although successful implantation in young patients have been described (Bergendal et al., 1991), the risk of failure is probably lower in adult patients. Problems such as growth, tooth development and eruption can be avoided, at any rate. On the other hand, implants used with orthodontic appliances can probably stimulate bone growth.

Another line of therapy with promising possibilities is the autotransplantation of teeth, as described in several case reports and studies (Eliassen et al., 1988; Lopes da Silveira et al., 1989). Both erupted and unerupted teeth were described as being successfully transplanted. Particularly in patients with a large number of missing teeth, the distribution of the missing teeth can be very unfavourable. This autotransplantation can be very useful for achieving a better distribution of the abutment teeth. In doing so a more or less ideal starting-point for dental therapy can

be created. Due to the underdevelopment of the alveolar process in patients with oligodontia, additional problems such as lack of retention of a (partial) prosthesis can be expected. Therefore, autotransplantation of unerupted teeth might, if available, be preferable. The alveolar process might response positively to the growth of the transplanted tooth germ. Research is needed to evaluate the possibilities of autotransplantation of teeth.

# Summary

Oligodontia, or congenitally missing teeth, is one of the anomalies a dental practitioner can be confronted with. Oligodontia has been the subject of several studies. Several anomalies are reported to be associated with oligodontia. These anomalies do not only concern the teeth; other symptoms are seen and other organs can be affected. Therefore, establishing a correct diagnosis in these patients is complicated.

In the Netherlands, patients with oligodontia, or congenitally missing teeth, never have never been the subject of an extensive study. In this thesis the clinical, radiographic and genetic aspects of oligodontia are evaluated in Dutch patients with oligodontia.

In **Chapter 1**, a brief introduction is given concerning oligodontia. The relevance of the problem is described and the aims of the study are given. Finally, operational definitions concerning the anomaly are presented. Patients with oligodontia indicated that the information concerning the anomaly given to them by general practitioners was concise. The patients and their parents want to be informed about the nature of the disorder and what to expect in the next generation.

The aims of the study were i) to define the symptoms occurring in a Dutch population of patients with oligodontia and ii) to make a contribution to the mode of inheritance. This knowledge will enable the dental practitioner to make the diagnosis "congenitally missing teeth". Furthermore, the dental practitioner will be able to inform his patients about the nature and severity of their disorder.

Oligodontia was defined as the congenital missing of six or more teeth excluding the third molars.

In **Chapter 2**, a review of literature is presented. One can see from the literature review that no consensus exists concerning the definition of oligodontia. The prevalence varies from 2.3% to 10.1%, as reported by several authors. Characteristic dental and oral symptoms reported are, among others, congenitally missing teeth, a reduction in the size and form of teeth, a reduction in size and form of the alveolar process, a delay in tooth formation and anomalies of the enamel (Table 2.3).

Oligodontia can also occur as one of the features of a syndrome. Syndromes described, among others, are ectodermal dysplasia, clefts, Rieger syndrome and Ellis-Van Creveld syndrome. Features of these syndromes are, for example, hypotrichosis, hypohidrosis, syndactyly and others.

Furthermore, the etiological factors of oligodontia are reviewed in this Chapter. Important environmental factors known to contribute to oligodontia are roentgen and radium rays, traumas, lues congenita and many others. Heredity is one of the most important etiological factors given in literature. Both single gene and multifactorial inheritance are described as being responsible for oligodontia.

Finally, a discussion of the literature review is presented. When taking the literature review into account, the conclusion can be made that the aims as established in Chapter 1 were correct.

In **Chapter 3**, a brief introduction is given concerning the participants and

instruments used in this study. A total of 332 patients with oligodontia participated in this study. Control groups were derived partly from literature and part of the data were collected by examining the controls and the available orthopantomograms. Instruments used were: i) a clinical history; ii) a family history questionnaire and iii) the procedure of patient documentation.

After informing the patient about the study an appointment was made for the clinical examination. Following this examination, the family history questionnaire was given to the patient.

In **Chapter 4**, the prevalence and distribution of congenitally missing teeth in the Netherlands is discussed. The prevalence of oligodontia was recorded in 37 dental practices in the Netherlands. A prevalence of 0.08% (1:1250) was found for oligodontia.

In a population of 196 patients with isolated oligodontia (oligodontia/I) and oligodontia as part of a syndrome (oligodontia/S) the distribution of missing teeth was recorded. Patients with oligodontia/S were missing significantly ($P < 0.01$) more teeth than those with oligodontia/I. The difference between males and females with oligodontia/S was significant ($P < 0.01$). The difference between males and females with oligodontia/I, though, was not significant. The difference in distribution of missing teeth over maxilla/mandible and left/right sides was not significant. One could conclude, in order to obtain accurate information on patients with oligodontia, the two groups should be evaluated separately, if the number of missing teeth is taken into consideration.

In **Chapter 5**, the measurements from dental casts, mesiodistal dimensions and the morphological changes of teeth are described. The aims of this part of the study were to evaluate i) the gradient of reduction in tooth size and ii) the changes in tooth morphology.

The mesiodistal dimensions of the teeth were measured on 82 casts. Nearly all differences found when comparing the mesiodistal dimensions of teeth of patients with oligodontia with data of the control-group were significant differences ($P < 0.01$ and $P < 0.001$). It was discovered that, with an increase in number of missing teeth, a decrease could be perceived of the mesiodistal dimension.

Furthermore, there were signs of reduction in tooth morphology. A reduction in number of cusps was found in molars as was a reduction in height of cusps of premolars. The conical form of the teeth was not limited only to the lateral incisors as often described in literature, but premolars showed a conical form as well.

The results support the hypothesis that oligodontia is not an isolated phenomenon but a complex of other dental changes.

In **Chapter 6**, the radiological findings from patients with oligodontia are presented. The aims of this part of the study were to evaluate i) tooth formation; ii) the occurrence of taurodontism and iii) length of teeth in patients with oligodontia.

The calcification stages of the teeth on the left side of the lower jaw were rated. A comparison was made with a control group matched for race, sex and age. In patients with oligodontia, a tendency to show delayed tooth formation was found. Significant differences in tooth formation were found in several stages of the teeth, between males with oligodontia and the control group. In females, only stage 5 of the second mandibular molar showed a significant difference. Because of the great individual variation in tooth formation between patients with oligodontia the tooth

formation of each patient with oligodontia should be individually examined before starting treatment.

Taurodontism and a reduced length are reported to occur in patients with oligodontia. The aim of this part of the study was to evaluate the occurrence of taurodontism as well as the length of the teeth in Dutch patients with oligodontia. Panoramic radiographs of 117 patients with oligodontia and 91 controls were collected. Taurodontism of the mandibular first molars was recorded and the length of canines, premolars and first molars of the mandible were measured.

In patients with oligodontia, 28.9% showed taurodontism of one or two mandibular first molars. The prevalence of taurodontism in normal Dutch subjects was 9.9%. No significant differences were found between the two sexes in both groups or between the unilateral and bilateral occurrence of taurodontism.

Oligodontia is often associated with other ectodermal defects. The present findings of higher percentages of taurodontic molars in patients with oligodontia supported the hypothesis that taurodontism may result from an ectodermal defect and a manifestation of developmental instability in patients with oligodontia.

The length of mandibular canines and first molars in females were significantly reduced. In males, only the lower right first molar showed significant reduction. The reduced length of the teeth may also be the result of a defect in ectodermal cells. Both taurodontism and reduced length are of importance when considering dental therapy.

In **Chapter 7**, oral and extra-oral symptoms and associations between combinations of these symptoms are given. Aim of this part of the study was to identify the association of patterns of congenitally missing teeth with combinations of ectodermal symptoms occurring in patients with oligodontia.

For this study, 167 patients with oligodontia, both isolated and as part of a syndrome, and 135 healthy controls were interviewed and documented.

During the study, it appeared that patients with oligodontia/I also showed minor symptoms of ectodermal dysplasia, leading to the question of whether selecting a group of patients with oligodontia/I was justified. No significant differences were found between the control group and the patients with isolated oligodontia, with the exception of differences in the skin. This would indicate, then, that selecting a group of patients with oligodontia/I was indeed justified.

It could be concluded from the present study that there were no clear associations between congenitally missing teeth, either individually or patterns, or between the ectodermal symptoms or combinations of ectodermal symptoms.

However, if the most stable teeth are missing, or if a large number of teeth are missing, one could conclude that the patient should be carefully examined for symptoms of ectodermal dysplasia.

In **Chapter 8**, environmental and genetic factors as found in a population of Dutch patients with oligodontia were described. The aims of this part of the study were i) to establish a reduction in tooth size in relatives of patients with oligodontia and iii) to make a contribution to the knowledge of the possible mode of inheritance of patients with isolated oligodontia.

From the present study, the conclusion could be made that no obvious causative environmental factors existed in the population studied.

Measurements of the mesiodistal dimensions of the relatives revealed significant

reductions in certain teeth, even in those relatives with a full permanent dentition. This indicates again, that the reduction in size of teeth may be a minor expression of congenitally missing teeth.

The mode of inheritance was in close agreement with an AD inheritance. A reduced penetrance of 69% was found. The striking observation was made that a difference was found in the analysis of the mode of inheritance between groups of patients with 6 or more missing teeth and groups missing less than six teeth. This would indicate that the chosen limit was not a purely theoretical one.

In **Chapter 9**, crown-size profile patterns of patients with oligodontia were compared with the crown-size profile patterns of patients with Down syndrome, 45,X/46,XX females, patients with cleft lip and palate and female carriers of X-linked ectodermal dysplasia.

In patients with oligodontia both early and late-developing teeth were severely affected, compared with patients with other syndromes. In patients with Down syndrome, only late-developing teeth were severely affected and in females with 45,X/46,XX mosaicism only early-developing teeth were severely affected.

The crown-size profile patterns of patients with oligodontia were comparable to those of patients with cleft lip and palate.

In all groups, left-right asymmetry was reported, indicating a developmental instability.

The results of this part of the study supported the hypothesis that the congenital missing of teeth and cleft lip and palate are probably the result of the same etiological factor.

In **Chapter 10**, the methods and results of the study are discussed. A diagnostic scheme for the general practitioner is presented. Using logistic regression a patient could be classified as having isolated oligodontia or oligodontia as part of a syndrome with a specificity and sensitivity of 88.2%.

The results of the study, taking into account the following definitions to be used in future research are given:

| | |
|---|---|
| ***Hypodontia/I:*** | *the congenital missing of less than six teeth, excluding the third molars.* |
| ***Hypodontia/S:*** | *the congenital missing of less than six teeth, excluding the third molars, as part of a syndrome.* |
| ***Oligodontia/I:*** | *the congenital missing of six or more teeth, excluding the third molars.* |
| ***Oligodontia/S:*** | *the congenital missing of six or more teeth, excluding the third molars, as part of a syndrome.* |
| ***Anodontia/I:*** | *the congenital missing of all deciduous and/or permanent teeth.* |
| ***Anodontia/S:*** | *the congenital missing of all deciduous and/or permanent teeth, as part of a syndrome.* |

When not discussing one of the groups in particular, the use of the term congenitally missing teeth is appropriate.

Finally, recommendations are given for future research.

# Samenvatting

Oligodontie, ofwel het niet aangelegd zijn van gebitselementen, is één van de aangeboren afwijkingen waar een algemeen practicus mee geconfronteerd kan worden. In vele studies zijn de verschillende aspecten van de oligodontie onder de loupe genomen. Er is een aantal afwijkingen bekend die voorkomen in associatie met oligodontie. Het betreft niet alleen afwijkingen aan de gebitselementen, ook andere organen en systemen kunnen aangedaan zijn. Dit maakt het stellen van een correcte diagnose bij deze categorie patiënten gecompliceerd.

In Nederland is geen uitgebreid onderzoek verricht naar het niet aangelegd zijn van gebitselementen ofwel oligodontie. In dit proefschrift worden de klinische, röntgenologische en genetische aspecten van Nederlandse oligodontiepatiënten geëvalueerd.

In **Hoofdstuk 1** wordt na een korte introductie, de problematiek van de oligodontiepatiënten beschreven. De patiënten geven aan dat over het algemeen de informatie die zij van de algemeen practicus ontvangen gering is. De patiënten en/of de ouders van de patiënten willen graag meer uitgebreid geïnformeerd worden omtrent de ernst van de afwijking en over datgene wat ze in een volgende generatie kunnen verwachten.

Het doel van dit onderzoek was het definiëren van de symptomen zoals die gesignaleerd worden bij patiënten met oligodontie, als ook een bijdrage leveren aan de kennis omtrent de wijze van overerving. Deze kennis zal de algemeen practicus beter in staat stellen de diagnose "niet aangelegde gebitselementen" te stellen. Tevens zal de algemeen practicus over meer informatie kunnen beschikken om de patiënt te informeren over de ernst van de aandoening en wat de risico's zijn voor het aangedaan zijn van een individu in een volgende generatie.

Oligodontie wordt in dit onderzoek gedefinieerd als het niet aangelegd zijn van 6 of meer gebitselementen, uitgezonderd de derde molaren.

In **Hoofdstuk 2** wordt een overzicht gegeven van de literatuur. Het blijkt dat er allesbehalve eenduidigheid is over de definitie van oligodontie. Ook de prevalentie varieert sterk van 2.3% tot 10.1%. De belangrijkste tandheelkundige en orale symptomen zijn: het niet aangelegd zijn van de gebitselementen, een gereduceerde vorm en grootte van de gebitselementen, een gereduceerde vorm van de processus alveolaris, vertraagde ontwikkeling van de gebitselementen en afwijkingen aan het glazuur (Tabel 2.3).

Oligodontie wordt ook regelmatig vermeld als één van de symptomen van een syndroom. In dit literatuuroverzicht worden o.a. beschreven: ectodermale dysplasie, gespleten lip en/of gehemelte, Rieger syndroom en Ellis-Van Creveld syndroom. Symptomen zoals ze voorkomen in de verschillende syndromen zijn o.a. hypotrichose, hypohidrose en syndactylie.

Vervolgens worden de belangrijkste etiologische factoren beschreven. Röntgenstraling, trauma en lues congenita zijn enkele omgevingsinvloeden die genoemd zijn in de literatuur met betrekking tot het ontstaan van oligodontie. De genetische invloeden worden echter als de belangrijkste oorzaak aangemerkt van het niet aangelegd zijn van de gebitselementen. Zowel de Mendeliaanse wijze van

overerving als multifactoriële overerving worden beschreven.

Tenslotte volgt er een discussie over het gepresenteerde overzicht, welke leidt tot de conclusie dat de vraagstellingen in dit proefschrift terecht zijn.

In **Hoofdstuk 3** worden de verschillende patiëntengroepen en de formulieren zoals gebruikt in het onderzoek, geïntroduceerd. In totaal hebben 332 oligodontiepatiënten aan het onderzoek deelgenomen. De controlegroepen zijn gedeeltelijk afkomstig uit de literatuur en gedeeltelijk verkregen uit eigen onderzoek. Tenslotte worden in dit hoofdstuk de gebruikte instrumenten geïntroduceerd.

In **Hoofdstuk 4** worden de mogelijke prevalentie en de verdeling van de ontbrekende gebitselementen van de Nederlandse populatie gepresenteerd. In 37 Nederlandse tandarts-praktijken werd de prevalentie van oligodontie geschat. De frequentie was 0.08% ofwel 1:1250 patiënten.

Uit de verdeling van ontbrekende gebitselementen bleek dat patiënten met oligodontie als onderdeel van een syndroom gemiddeld meer gebitselementen niet aangelegd hebben dan patiënten met geïsoleerde oligodontie. Uitgesplitst naar geslacht bleek er wel een verschil te zijn tussen de mannen en vrouwen met oligodontie als onderdeel van een syndroom maar niet tussen mannen en vrouwen met geïsoleerde oligodontie. De verschillen in de verdeling over links en rechts en boven en onder bleken niet significant.

Hieruit mag worden afgeleid dat als er gekeken wordt naar het aantal ontbrekende gebitselementen het noodzakelijk is onderscheid te maken tussen patiënten met oligodontie als onderdeel van een syndroom en geïsoleerde oligodontie.

In **Hoofdstuk 5** worden de metingen beschreven zoals die zijn verricht op de gebitsmodellen, mesiodistale afmetingen en morfologische veranderingen. Het doel van dit deel van het onderzoek was het vaststellen van de graad van reductie van de mesiodistale afmetingen en de veranderingen in morfologie. Er waren 82 gebitsmodellen beschikbaar.

Vrijwel alle gebitselementen van de oligodontiepatiënten waren significant smaller dan die van de controlegroep. Het bleek zelfs zo te zijn dat hoe meer gebitselementen er ontbreken, hoe smaller de gebitselementen zijn die wel zijn aangelegd.

Naast de gereduceerde mesiodistale afmetingen werd een reductie in het aantal knobbels van de molaren waargenomen. De premolaren vertoonden een reductie in hoogte van de knobbels met name de palatinale en linguale knobbels. Uiteraard werden in deze populatie ook de veel beschreven conische gebitselementen waargenomen. Zelfs de premolaren vertoonden deze coniciteit.

De resultaten bevestigen de hypothese dat oligodontie niet een geïsoleerd fenomeen is, maar dat zij is gerelateerd aan een complex van andere tandheelkundige afwijkingen.

In **Hoofdstuk 6** worden de radiologische bevindingen bij oligodontiepatiënten beschreven. Het doel van dit deel van het onderzoek was het vaststellen van een eventuele vertraging in de ontwikkeling van de gebitselementen, het voorkomen van taurodontisme en het beoordelen van de lengte van de gebitselementen.

Bij 216 patiënten werd het calcificatiestadium van de aanwezige gebitselementen vastgelegd. De resultaten werden vergeleken met gegevens uit het Nijmeegs groeionderzoek.

Bij de oligodontiepatiënten was een neiging naar een vertraagde ontwikkeling van

de gebitselementen waarneembaar. Echter, deze vertraging was slechts bij een gering aantal stadia significant in vergelijking met de data van het Nijmeegs groeionderzoek. Dit verschil kwam met name tot uiting bij jongens.

Uit dit onderzoek bleek dat er onderling grote verschillen waarneembaar zijn bij de oligodontiepatiënten. De verschillen bij de controlegroep bleven beperkt tot de normale, biologisch, te verwachten spreiding.

Taurodontisme en een gereduceerde lengte worden wel beschreven als zijnde geassocieerd met oligodontie. In deze studie werden 117 OPG's van patiënten vergeleken met die van een controlegroep. De eerste molaren in de onderkaak werden beoordeeld op de aanwezigheid van taurodontisme. De cuspidaten, premolaren en eerste molaar in de onderkaak werden gebruikt voor de lengtemetingen.

Van de oligodontiepatiënten vertoonden 28.9% taurodontisme van één of twee ondermolaren. De prevalentie van taurodontisme in de controlegroep was 9.9%.
Er waren geen verschillen in het voorkomen van taurodontisme tussen mannen en vrouwen. Taurodontisme kwam zowel unilateraal als bilateraal voor.

Taurodontisme wordt beschreven als zijnde het resultaat van een ectodermaal defect en een aanwijzing van instabiliteit in de ontwikkeling. De associatie van oligodontie en andere ectodermale verschijnselen en de verhoogde aanwezigheid van taurodontisme ten opzichte van een controlegroep ondersteunden deze hypothese.

De gereduceerde lengte van de gebitselementen was mogelijk ook het resultaat van een defect in de ectodermale cellen. Significant gereduceerd ten opzichte van de controlegroep waren de cuspidaten en eerste molaren bij vrouwen; bij mannen was dit alleen de eerste molaar rechtsonder.

Zowel taurodontisme als de lengte van de gebitselementen zijn van invloed op de tandheelkundige behandeling.

In **Hoofdstuk 7** worden de orale en extra-orale symptomen en de associatie tussen combinaties van deze symptomen gepresenteerd. Het doel van dit onderzoek was het vaststellen van verbanden tussen combinaties van ontbrekende gebitselementen en combinaties van ectodermale symptomen zoals die voorkomen bij oligodontiepatiënten.

Voor dit onderzoek werden 167 patiënten met oligodontie en 135 controle personen geïnterviewd en gedocumenteerd.

Tijdens het onderzoek bleek dat ook de patiënten met geïsoleerde oligodontie verschijnselen van ectodermale dysplasia vertoonden. Bij vergelijking van de extra-orale verschijnselen van de geïsoleerde oligodontiepatiënten met de controlegroep werden echter geen significante verschillen gevonden met uitzondering van de huid. Het lijkt daarom correct te spreken van geïsoleerde oligodontie.

Er werden geen directe samenhangen geconstateerd tussen de combinaties van ontbrekende gebitselementen en de ectodermale symptomen. Duidelijk was echter dat men alert moet zijn op ectodermale symptomen als de meest stabiele gebitselementen niet zijn aangelegd of als er sprake is van een groot (> 12) aantal ontbrekende gebitselementen.

In **Hoofdstuk 8** wordt het voorkomen van exogene factoren en genetische analyses beschreven. Het doel van dit onderzoek was ten eerste het vaststellen van een eventuele reductie van de gebitselementen van familieleden en ten tweede een bijdrage te leveren aan de kennis omtrent de wijze van overerving van geïsoleerde

oligodontie.

Uit het onderzoek kwamen geen duidelijke omgevingsinvloeden naar voren die als oorzaak van oligodontie konden worden aangewezen.

De metingen van de mesiodistale afmetingen van de gebitselementen van de familieleden gaven een reductie te zien van gebitselementen bij familieleden met een compleet permanente dentitie. Dit geeft eens te meer aan dat de reductie in grootte moet worden gezien in samenhang met het niet aangelegd zijn van gebitselementen.

Bij de 50 geanalyseerde stambomen was een autosomaal dominante wijze van overerving het meest waarschijnlijk. De stambomen voldeden niet aan de criteria voor multifactoriële overerving. Tenslotte was opmerkelijk dat de grens van minder dan 6 niet aangelegde gebitselementen en 6 of meer niet aangelegde gebitselementen, niet alleen een theoretische grens leek te zijn, maar ook betekenis heeft bij het analyseren van de wijze van overerving.

In **Hoofdstuk 9** worden de patronen van reductie van de grootte van de gebitselementen van oligodontiepatiënten vergeleken met die van patiënten met het Down syndroom, 45,X/46,XX mosaicisme, gespleten lip en gehemelte en draagsters van X-gebonden ectodermale dysplasie.

Bij patiënten met het Down syndroom zagen we een reductie in grootte van de laat ontwikkelende gebitselementen. Bij 45,X/46,XX mosaïcisme zagen we daarentegen een reductie in grootte bij de gebitselementen die in een vroeg stadium worden aangelegd. Bij oligodontiepatiënten waren zowel de vroeg als laat ontwikkelende gebitselementen aangedaan. Dit kwam overeen met de patiënten met gespleten lip en gehemelte.

In alle groepen werd een links-rechts asymmetrie waargenomen. Dit duidt op een instabiele ontwikkeling. De resultaten bevestigden de hypothese dat het niet aangelegd zijn van gebitselementen en gespleten lip en gehemelte mogelijk het resultaat zijn van dezelfde etiologische factor.

In **Hoofdstuk 10** tenslotte worden de gebruikte methoden en de resultaten van dit onderzoek onder de loupe genomen. Voor de algemeen practicus werd een schema gegeven waarmee onderscheid gemaakt kan worden tussen geïsoleerde oligodontie en oligodontie als onderdeel van een syndroom met een specificiteit en sensitiviteit van 88.2%.

Aan de hand van dit onderzoek werden de volgende definities aanbevolen:

| | |
|---|---|
| ***Hypodontie/I:*** | *het niet aangelegd zijn van minder dan 6 gebitselementen, uitgezonderd de derde molaren.* |
| ***Hypodontie/S:*** | *het niet aangelegd zijn van minder dan 6 gebitselementen, uitgezonderd de derde molaren; als onderdeel van een syndroom.* |
| ***Oligodontie/I:*** | *het niet aangelegd zijn van 6 of meer gebitselementen, uitgezonderd de derde molaren.* |
| ***Oligodontie/S:*** | *het niet aangelegd zijn van 6 of meer gebitselementen, uitgezonderd de derde molaren, als onderdeel van een syndroom.* |

*Anodontie/I:* *het niet aangelegd zijn van de complete melk- en/of permanente dentitie.*

*Anodontie/S:* *het niet aangelegd zijn van de complete melk- en/of permanente dentitie, als onderdeel van een syndroom.*

Als niet specifiek gesproken werd over één van de hierboven genoemde groepen, werd aanbevolen de term "niet aangelegd zijn van gebitselementen" te gebruiken.

Het onderscheid tussen "als onderdeel van een syndroom" en "geïsoleerd" werd aangegeven door middel van de extensies /I (geïsoleerd) en /S (als onderdeel van een syndroom).

Wanneer men de wijze van overerving onderzoekt, is het van belang het gereduceerd zijn van de gebitselementen mee te nemen als ook het niet aangelegd zijn van de derde molaren. Beide zijn uitingen van het niet aangelegd zijn van gebitselementen.

Tenslotte werden aanbevelingen gedaan voor verder onderzoek.

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# Appendix 1
# List of syndromes in which oligodontia is one of the common features, as well as one of the incidental features

Definitions:

| | |
|---|---|
| Oligodontia: | The congenital missing of six or more teeth, excluding the third molars. |
| Hypodontia: | The congenital missing of less than six teeth, excluding the third molars. |

The most important sources from which the syndromes with congenitally missing teeth were derived are:
Gorlin et al. (1990) Syndromes of the Head and Neck (3rd ed.)
McKusick (1990) Mendelian inheritance in man (9th ed.)
Buyse (1990) Birth Defects Encyclopedia

McK: Number as noted in McKusick, VA (1990): Mendelian inheritance in man. Catalogue of autosomal dominant, autosomal recessive, and X-linked phenotypes.
Example: Mck 129900*: Pattern of inheritance certain, according to the McKusick

**The references given are of those papers that are informative on congenitally missing of teeth specifically.**

Contents:
Mode of inheritance:
- Several modes of inheritance are reported
  - hypodontia
  - oligodontia
- Autosomal dominant
  - hypodontia
  - oligodontia
- Autosomal recessive
  - hypodontia
  - oligodontia
- X-linked recessive
  - hypodontia
  - oligodontia
- X-linked dominant
  - hypodontia
  - oligodontia
- Unknown
- Chromosomal

## Mode of inheritance: Several modes of inheritance are reported.

**Hypodontia:**

- **BD syndrome** (Neuhauser et al., 1975)
  Includes: Multiple congenital anomalies - Mental retardation - Athetoid cerebral palsy
- **Cutis gyratum with acanthosis nigricans** (Stevenson et al., 1978)
  Includes: Beare-Stevenson syndrome, Cutis gyratum syndrome
- **Ectodermal dysplasia - Alopecia - Mental retardation** (Bartalos, 1968)
- **Growth hormone deficiency - Wormian bones - Dextrocardia -Brachycamptodactyly - other midline defects** (Stratton and Parker, 1989)
- **Ichthyosis - Deafness - Brachydactyly** (Ruzicka et al., 1981)
- **Olmsted - Palmoplantar keratoderma plus** (Poulin et al., 1984)

**Oligodontia:**

- **Cleft lip/palate, with split hand or foot** (Gorlin et al., 1971a)
- **Hypothyroid - Dermoid Cysts - Cleft palate - Dry skin** (Zadik et al., 1983)
- **Pilo-dento-ungular dysplasia with microcephaly** (Tajara et al., 1987)
  Includes: Ectodermal dysplasia, pilo-dento-ungular type
  According to Gorlin et al. (1990): Hair - nail - skin - teeth dysplasias; Dermo-odonto-dysplasia; Odonto-onychial-dermal dysplasia; Odonto-onychial-dysplasia; Tricho-dermo-dysplasia with dental alterations
- **Premature aging - Microcephaly - Unusual facies - Multiple nevi and mental retardation** (Baraitser et al., 1988)
  Includes: Mulvihill syndrome
- **Tricho-odonto-onycho-dermal dysplasia** (Pinheiro et al., 1981)

## Mode of inheritance: Autosomal dominant

**Hypodontia:**

- **Asymmetric crying facies** (Silengo et al., 1986)
  Includes: Hypoplasia of depressor anguli oris muscle; Cayler syndrome; Partial unilateral facial paresis; Cardiofacial syndrome
  McK 125520*
- **Cherubism** (Sedano et al., 1977)
  Includes: Intraosseous fibrous swelling of the jaw
  McK 118400*
- **Clefting - Premaxilla agenesis** (Martin et al., 1977)
- **Cornelia de Lange syndrome** (Yamamoto et al., 1987)
  Includes: Brachmann - de Lange syndrome; Typus degenerativus amstelodamensis
  McK 122470
- **Crouzon craniofacial dysostosis** (Kollar et al., 1988)
  Includes: Crouzon disease; Crouzon syndrome; Craniofacial dysostosis
  McK 123500*
- **Holoprosencephaly** (Johnson, 1989)
  Includes: Midline cleft syndrome, DeMeyer sequence included; Arhinencephaly; Cebocephaly; Ethmocephaly
  McK 157170
- **Hypertrichosis universalis** (Witkop, 1975)
  Includes: Hypertrichosis lanuginosa congenita
  McK 145700*

- **Monilethrix** (Witkop, 1975)
  McK 15800*
- **Oculo-auriculo-vertebral spectrum** (Farias and Vagervik, 1988)
  Includes: AOV syndrome; Goldenhar syndrome; Hemifacial microsomia
  McK 164210
- **Oculodentodigital syndrome** (Patton and Laurence, 1985)
  Includes: ODD syndrome; Oculodentoosseous dysplasia (ODOD)
  McK 164200*
- **Oromandibular limb hypogenesis syndromes** (Gorlin et al., 1990)
  * **Glossopalatine ankylosis syndrome, type III** (Chiacarelli and Palayes, 1985)
  * **Hanhart syndrome, type V** (Test et al., 1976)
    Includes: Congenital micrognathia and partial adactylia
    McK 103300
  * **Hypoglossia - hypodactylia, type II** (Gima et al., 1987)
    Includes: Aglossia - adactylia syndrome; Ankyloglossum superior syndrome
    McK 103300
- **Osteogenesis imperfecta, type I** (Lukinmaa et al., 1987)
- **Otodental syndrome** (Salinas et al., 1988; pp. 141, 213)
  McK 166750*
- **Palmoplantar hyperkeratosis - Short stature - Facial dysmorphism - Hypodontia** (Seow, 1989)
- **Saethre-Chotzen syndrome** (Freire-Maia and Pinheiro, 1984; pp. 27)
  Includes: Acrocephalo syndactyly type III syndrome (ACS III); Chotzen syndrome; Acrocephaly, Skull asymmetry and mild syndactyly
  McK 101400*
- **Short stature - Characteristic facies - Mental retardation - Skeletal anomalies-Macrodontia** (Tollaro, 1984)
  Includes: KBG syndrome; Cranio-oculo-dental syndrome
  McK 148050*
- **Singleton - Merten syndrome** (Gay and Kuhn, 1976)
  Includes: Skeletal defects with aortic calcification and muscle weakness; Idiopathic calcification of aorta, dental and bone defects
  McK 182250*
- **Sparse hair - Hypoplasia thumbs - Single central maxillary incisor** (Winter et al., 1988)
  Includes: Single central maxillary incisor; Mono-supero-centro-incisivo-dontic dwarfism; Solitary maxillary central incisor and short stature
  McK 147250
- **Tooth and nail syndrome** (Hudson and Witkop, 1975)
  Includes: Hypodontia and nail dysgenesis; Dysplasia of nails with hypodontia; Witkop tooth - nail syndrome
  McK 189500*
- **Van der Woude syndrome** (Ranta and Rintala, 1983)
  Includes: Lip-pit syndrome; Cleft lip and/or palate with mucous cysts of lower lip; Lip pits or mounds and cleft lip or palate; Cleft lip - palate and paramedian sinuses of the lower lip
  McK 119300*
- **Weijers acrofacial dysostosis** (Roubicek and Spranger, 1984)
  Includes: Acrodental dysostosis of Weijers; Curry-Hall syndrome
  Weijers syndrome; Acrodental dysostosis; Acrofacial dysostosis; Acrofacial postaxial defect syndrome
  McK 193530*

- **Williams-Beuren syndrome** (Boraz, 1991)
  Includes: Williams syndrome; Elfin facies with hypercalcemia; Idiopathic hypercalcemia; Infantile hypercalcemia; Supravalvular aortic stenosis; Hypercalcemia - peculiar facies - supravalvular aortic stenosis
  McK 194050*

<u>Oligodontia:</u>

- **Ankyloblepharon - Ectodermal dysplasia - Cleft lip and palate** (Green et al., 1987)
  Includes: AEC-syndrome; Hay-Wells syndrome
  McK 106260
- **Apert syndrome** (Schudy, 1984)
  Includes: Acrocephalosyndactyly, type I; Apert-Crouzon disease; Vogt cephalosyndactyly; Acrocephalosyndactyly, type II
- **Böök - syndrome** (Böök, 1950)
  Includes: PHC-syndrome; Premolar aplasia - Hyperhidrosis - Canities prematura; Hyperhidrosis, premature greying of the hair and premolar hypodontia
  McK 112300*
- **Cleft lip with or without cleft palate** (Gorlin, 1970)
  Includes: Nonsyndromic orofacial cleft
  McK 119530*
- **Cleft lip-palate - Hypohidrosis - Thin wiry hair - Dystrophic nails - hypospadias and oligodontia** (Santos et al., 1990)
  Includes: Rapp-Hodgkin ectodermal dysplasia hypohidrotic- Cleft lip/palate-Ocular, Genital, Digital anomalies; Ectodermal dysplasia, anhidrotic with cleft lip and cleft palate; Wiry uncombable straw-like hair, palate/lip anomalies
  McK 129400*
- **Dermo-odonto-dysplasia** (Pinheiro and Freire-Maia, 1983a)
  McK 125640
- **Ectodermal dysplasia with tricho-odonto-onychial dysplasia** (Tsakalakos et al., 1986)
  McK 129510
- **Ectodermal dysplasia - Deafness - Ocular anomalies** (Witkop, 1975)
  Includes: Marshall syndrome; Deafness, myopia, cataract, saddle nose, Marshall type; Myopia, cataract, saddle nose, hypertelorisme, short stature and deafness
  McK 154780*
- **Ectodermal dysplasia** (Freire-Maia and Pinheiro, 1984; pp. 47-50)
  Includes: Zanier - Roubicek - Ectodermal dysplasia
  McK 129490
- **Ectodermal dysplasia - Cataract - Retinal dystrophy** (Bork et al., 1987)
- **Ectodermal dysplasia hypohidrotic** (Bocian and Rimoin, 1979)
- **Ectodermal dysplasia** (Jorgenson et al., 1987)
  McK 129490
- **Ectrodactyly - Ectodermal dysplasia without cleft lip/palate** (Wallis, 1988)
  MCK 129810
- **Ectrodactyly - Ectodermal dysplasia - Cleft lip/palate** (Rodini and Richeiro-Costa, 1990)
  Includes: EEC-syndrome; Ectrodactyly, Ectodermal dysplasia, Clefting syndrome
  McK 129900*
- **Johnson neuroectodermal syndrome** (Johnston et al., 1987)
  Includes: Alopecia - Anosmia - Deafness - Hypogonadism syndrome (AADH)
  McK 147770

- **Lacrimo-auriculo-dento-digital syndrome** (Kreutz and Hoyme, 1988)
  Includes: LADD syndrome; Levy-Hollister syndrome; Limb malformations, dento-digital syndrome
  McK 149730*
- **Oligodontia - Microcephaly - Short stature - Characteristic facies** (Gorlin et al., 1990).
- **Progeria** (Hasty and Yann, 1988)
  Includes: Hutchinson- Gilford progeria syndrome
  McK 176670
- **Rieger syndrome** (Childers and Wright, 1986)
  Includes: Iridogoniodysgenesis with somatic anomalies; Hypodontia and primary mesodermal dysgenesis of the iris
  McK 180500*
- **Temtamy - McKusick - Syndactyly - Skeletal dysplasia** (Temtamy and McKusick, 1978)
  Includes: Ulnar- Mammary (Pallister); Schinzel syndrome
  McK 181450*
- **Trichodental dysplasias** (Kersey, 1987)
- **Tricho-dermo-dysplasia - Dental anomalies** (Pinheiro et al., 1986)

## Mode of inheritance: Autosomal recessive

**Hypodontia:**
- **Aganglionic megacolon and cleft lip and/or palate** (Goldberg and Shprintzen, 1981)
  Includes: Hirschsprung - Cleft palate - Mental retardation; Hirschprung disease
  McK 249200
- **Bloom syndrome** (German, 1969)
  Includes: Growth deficiency - Facial erythema - Chromosome instability
  McK 210900*
- **Cleft lower lip - Chorioretinal degeneration** (Maumenee, 1977)
  Includes: Maumenee syndrome
- **Dysosteosclerosis** (Houston et al., 1978)
  Includes: Albers-Schonberg syndrome; Osteosclerosis - Platyspondyly
  McK 224300*
- **Gorlin - Chaudry - Moss syndrome** (Gorlin, 1985)
  Includes: Gorlin syndrome; Craniofacial dysostosis, hypertrichosis, hypoplasia of labia majora, dental and eye anomalies, patent ductus arteriosis, normal intelligence
  McK 233500
- **Ectodermal dysplasia - Cleft lip/ palate - Hand and foot deformity - Mental retardation** (Bowen and Armstrong, 1976)
  Includes: Clefting - Mental retardation - Ectodermal dysplasia Bowen-Armstrong syndrome; Rosselli-Gulienetti syndrome; Ectodermal dysplasia with cleft lip/palate and syndactyly
  McK 225000
- **Hypodontia - Sensorineural hearing loss - Dizziness** (Lee et al., 1978)
  Includes: Deafness - Oligodontia syndrome
  McK 221740
- **Keutel - syndrome** (Frijns et al., 1984)
  Includes: Brachytelephalangy - Pulmonary stenosis - Deafness; Pulmonic stenosis - Brachytelephalangism and calcification of cartilages
  McK 245150*

- **Leukomelanoderma - Infantilism - Mental retardation - Hypodontia and Hypotrichosis** (Berlin, 1961)
  Includes: Ectodermal dysplasia (Berlin form); Melanoleucoderma
  McK 246500
- **Monilethrix** (Witkop, 1975)
  McK 252200
- **Mulibrey nanism** (Myllärniemi et al., 1978)
  Includes: Pericardial constriction and growth failure; Dwarfism Mulibrey type; Dwarfism pericarditis
  McK 253250*
- **Oro-facial-digital syndrome type 2** (Torriello, 1988)
  Includes: OFD-2, Mohr syndrome
  McK 252100*
- **Pili torti (twisted hair)** (Nichamm, 1958)
  Includes: Pili torti - Enamel hypoplasia
  McK 261900
- **Polydactyly - Postaxial with dental and vertebral anomalies** (Rogers et al., 1977)
  Includes: Postaxial polydactyly - Dental - Vertebral syndrome; Rogers syndrome
  McK 263540
- **Scoliosis - Ulnar hypoplasia - Acromicria - Microcephaly - Mental retardation** (Cortada et al., 1982)
- **Walbaum - Dehaene - Schlemmer syndrome** (Walbaum et al., 1971)

<u>Oligodontia:</u>
- **Aredyld syndrome** (Pinheiro and Freire-Maia, 1983b)
  Includes: Acrorenal field defect - Ectodermal dysplasia - Lipoatrophic diabetes
  McK 207780
- **Brachymetapody - Anodontia - Hypotrichosis - Albinoid trait** (Tuomaala and Haapanen, 1968)
  Includes: Tuomaala-Haapanen; Oculoosteocutaneous syndrome; Anodontia - Hypotrichosis syndrome
  McK 211370
- **Cleft lip/palate - Ectodermal dysplasia - Hand/foot anomalies - Oligophrenia** (Gorlin et al., 1968)
  Includes: Popliteal pterygium syndrome; Popliteal pterygium, digital and genital anomalies; Facio-genito-popliteal syndrome
  McK 225000
- **Cleft palate - Microcephaly - Mental retardation - Musculoskeletal mass deficiency** (Weaver and Williams, 1977)
  Includes: Weaver-Williams syndrome; Cleft palate - Growth/mental retardation - Microcephaly and Unusual facies
- **Cleft lip/palate - Oligodontia - Syndactyly - Hair alterations** (Martinez et al., 1987)
  Includes: Zlotogora cleft lip/palate - Ectodermal dysplasia
- **Cleft palate - Stapes fixation - Oligodontia** (Gorlin, 1971b)
  McK 216300
- **Cranioectodermal dysplasia** (Salinas et al., 1984; pp. 216)
  Includes: Levin I syndrome; Sensenbrenner syndrome; Skeletal dysplasia - Sparse hair Dental anomalies
  McK 218330*
- **Deafness, congenital - Split hand and feet** (Raas-Rothschild et al., 1989)
  McK 220600

- **Dermatoosteolysis, kirghizian type** (Kozlova et al., 1983)
  Includes: Oligodontia - Keratitis - Skin ulceration - Arthroosteolysis; Kozlova - Altschuler - Kravchenko syndrome
  McK 221810
- **Eccrine tumours - Ectodermal dysplasia** (Nordin et al., 1988)
  McK 224750
- **Ectodermal dysplasia - Olivopontocerebellar degeneration** (Rushton and Genel, 1981)
- **Ectodermal dysplasia - Urticaria pigmentosa - Hypothyroidism** (Pinheiro et al., 1989)
- **Ectodermal dysplasia anhidrotic autosomal recessive** (Anton-Lamprecht, 1988)
  McK 224900*
- **Ectrodactyly - Ectodermal dysplasia - Macular dystrophy** (Olido et al., 1983)
  Includes: EEM-syndrome
  McK 225280*
- **Ellis-Van Creveld syndrome** (Himmelhoch and Mostofi, 1988)
  Includes: Chondroectodermal dysplasia
  McK 225500*
- **Epidermolysis bullosa simplex localisata** (Nielsen and Sjölund, 1985)
- **Facio-cardio-renal syndrome** (Eastman and Bixler, 1977)
  McK 227280
- **Fanconi syndrome** (Lau et al., 1988)
- **Hallermann - Streiff syndrome** (Friede et al., 1985)
  Includes: Oculo - Mandibulo - Dyscephaly and Hypotrichosis; Francois dyscephalic syndrome
  McK 234100
- **Johansson-Blizzard syndrome** (Zerres and Holtgrave, 1986)
  Includes: Nasal alar hypoplasia - Hypothyroidism - Pancreatic achylia - Congenital deafness; Malabsorption - Ectodermal dysplasia - Nasal alar hypoplasia; Ectodermal dysplasia - Exocrine pancreatic insufficiency
  McK 243800*
- **Lipoid proteinosis of Urbach and Wiethe** (Simpson, 1972)
  Includes: Lipoproteinosis, hyalinosis cutis et mucosae; Urbach-Wiethe disease; Lipoid proteinosis
  McK 247100
- **Medullary sponge kidney - Congenital absence of teeth** (Khoury et al., 1988)
- **Nail dystrophy - Deafness** (Robinson et al., 1962)
  Includes: Robinson ectodermal dysplasia; Ectodermal dysplasia and neurosensory deafness
  McK 224800
- **Odonto-onycho-dysplasia with alopecia (OODA)** (Pinheiro et al., 1985)
- **Oligodontia - Hypotrichosis - Palmoplantar hyperkeratosis - Apocrine hidrocystomas of eyelid margins** (Font et al., 1986)
  Includes: Schöpf syndrome
  McK 245000*
- **Pierre Robin - Cleft lower lip** (Ranta, 1984)
- **Pilodental dysplasia with refractive errors** (Kopysc et al., 1985)
  Includes: Euhidrotic ectodermal dysplasia; Trichodental dysplasia with hyperopia
  McK 262020
- **Pycnodysostosis** (Lacey et al., 1970)
  Includes: Maroteaux-Lamy syndrome
  McK 265800

- **Rothmund-Thomson syndrome** (Kraus and Gottlieb, 1970)
  Includes: Poikiloderma athrophicans and cataract
  McK 268400*
- **Skeletal dysplasia - Short Stature - Craniofacial anomalies** (Jones et al., 1986)
- **Taurodontism - Oligodontia - Sparse hair** (Stenvik et al., 1972)
  Includes: Congenital absence of teeth with taurodontia and sparse hair
  McK 272980
- **Tetramelic deficient ectodermal dysplasia - Deformed ears and other abnormalities** (Pavone et al., 1989)
  Includes: Odontotrichomelic tetramelic ectodermal dysplasia; Odontotrichomelic syndrome
  McK 273400
- **Tricho-odonto-onychial dysplasia** (Pinheiro et al., 1983c)
  Includes: Ectodermal dysplasia tricho-odonto-onychial type
  McK 275450
- **Wooly hair - Hypotrichosis - Everted lower lip and Outstanding ears** (Salamon et al., 1972)
  Includes: Salamon syndrome
  McK 278200

## Mode of inheritance: X-linked recessive

**Hypodontia:**
- **Coffin - Lowry syndrome** (Gilgenkrantz et al., 1988)
  Includes: Short stature - Head/face anomalies - Kyphoscoliosis - Retardation
  McK 303600*
- **Nance-Horan syndrome** (Bixler et al., 1984)
  Includes: Cataract dental syndrome; Brachydactyly - Oto-dental-cataract defects; Cataract - Oto - Dental defects
  McK 302350*
- **N syndrome** (Hess et al., 1974)
  Includes: Deafness - Spasticity - Dysmorphic facies; Hess syndrome
  McK 310465

**Oligodontia:**
- **Anhidrotic ectodermal dysplasia** (Clarke, 1987)
  Includes: X-linked hypohidrotic type; Christ-Siemens-Tourraine
  McK 305100*
- **Ectodermal dysplasia hypohidrotic - Focal sweating** (Gorlin, 1988)

## Mode of inheritance: X-linked dominant:

**Hypodontia:**
- **Oro-facial-digital syndrome Type 1** (Lauterstein and Pruzansky, 1969)
  Includes: Orofaciodigital syndrome, type 1; OFD-1; Pappillon - Léage - Psaume syndrome
  McK 311200*
- **Pallister W syndrome** (Pallister et al., 1974)
  Includes: Pallister - W - Clefting - Mental retardation - Skeletal defects; W syndrome
  McK 311450

Oligodontia:

- **Focal dermal hypoplasia** (Hall and Terezhalmy, 1983)
  Includes: Goltz-Gorlin; Goltz syndrome; Nevoid basal cell carcinoma syndrome
  McK 305600*
- **Frontometaphyseal dysplasia** (Fitzsimmons et al., 1982)
  Includes: Facio - Dental - Skeletal anomalies - Joint fractures - Hyperostosis
  McK 305620*
- **Incontinentia Pigmenti** (Fleischer-Peters and Ullman, 1982)
  Includes: Bloch- Sulzberger's syndrome; Incontinentia pigmenti type I
  McK 308300*
- **Oto-Palato-Digital syndrome (OPD, Type I)** (Gorlin et al., 1990)
  McK 311300*

## Mode of inheritance: Unknown

- **Hyperkeratosis palmaris - Deafness - Pili torti - Tooth anomalies**
  (Eyelund and Frontz, 1982)

## Mode of inheritance: Chromosomal

- **Klinefelter syndrome** (Darbyshire et al., 1989)
  Includes: Chromosome XXY; Hypergonadotropic hypogonadism
- **Trisomy 21** (Townsend, 1983)
  Includes: Down syndrome

# Appendix 2
# Pedigrees of patients with isolated oligodontia

Mode of inheritance

| | |
|---|---|
| ▪ Autosomal dominant | pedigrees 1-38 |
| theoretical alternative: | |
| X-linked dominant | pedigrees 28-33 |
| Autosomal recessive | pedigrees 34-38 |
| ▪ Autosomal recessive | pedigrees 39-42 |
| theoretical alternative: | |
| X-linked recessive | pedigree 42 |
| ▪ Sporadic cases | pedigrees 43-48 |
| ▪ Co-dominance | pedigrees 49-50 |

Legend pedigrees 1-50

| | |
|---|---|
| Males | |
| Females | |
| Not examined, no information available | |
| Parents | |
| Sibs | 1 2-4 5 |
| Not affected, examined by author | |
| Not affected, examined by dentist | |
| Not affected, not examined but reliable information from proband | |
| Congenitally missing teeth, examined by author | |
| Congenitally missing teeth, examined by dentist | |
| Congenitally missing teeth, not examined, but reliable information from proband | |
| Reduced form of the teeth, examined by author | |
| Reduced form of the teeth, examined by dentist | |
| Reduced form of the teeth, not examined, but reliable information from proband | |
| Number of congenitally missing teeth<br>? = number unknown | 18 ? |
| Proband | |
| Deceased | |

Pedigree 1
I
II
III

Pedigree 2
I
II
III

Pedigree 3
I
II
III

Pedigree 4
I
II
III

Pedigree 5
I
II
III
IV

Pedigree 6
I
II
III

Pedigree 7
I
II
III

Pedigree 8
I
II
III

Pedigree 9
I
II
III

Pedigree 10
I
II
III

Pedigree 11
I
II
III

Pedigree 12
I
II
III

Pedigree 13
I
II
III

Pedigree 14
I
II
III

Pedigree 15
I
II
III

Pedigree 16
I
II
III

Pedigree 17
I
II
III
IV

Pedigree 18
I
II
III

Pedigree 19
I
II
III

Pedigree 20
I
II
III

Pedigree 21
I
II
III

Pedigree 22
I
II
III

Pedigree 23
I
II
III

Pedigree 24
I
II
III

Pedigree 25
I
II
III

Pedigree 26
I
II
III

Pedigree 27
I
II
III

Pedigree 28
I
II
III

Pedigree 29
I
II
III

Pedigree 30
I
II
III

Pedigree 31
I
II
III
IV

Pedigree 32
I
II
III

Pedigree 33
I
II
III

Pedigree 34
I
II
III

Pedigree 35
I
II
III
IV

Pedigree 36
I
II
III

Pedigree 37
I
II
III

Pedigree 38
I
II
III

Pedigree 39
I
II
III

Pedigree 40
I
II
III

Pedigree 41
I
1 2 3 4
II
1 2 3 4-5
4 9
III
1 2 3

Pedigree 42
I
1 2 3 4
II
1 2
7 2
III
1 2 3

Pedigree 43
I
1 2 3 4
II
1 2 3-4
10
III
1 2

Pedigree 44
I
1 2 3 4
II
1-4 5 6 7-13
20
III
1-3 4

Pedigree 45
I
1 2 3 4
II
1 2 3 4-7
10
III
1-3 4

Pedigree 46
I
1 2
II
1 2
11
III
1-4 5

Pedigree 47
I
1 2
II
1 2
10
III
1 2

Pedigree 48
I
1 2 3 4
II
1-8 9 10 11-19
6
III
1 2

Pedigree 49
I
1 2 3 4
1 1
II
1 2
11 6
III
1 2 3

Pedigree 50
I
1 2 3 4
11 1 2
II
1 2 3 4 5
3 1 2 8
III
1 2 3 4 5

# Curriculum vitea

Yvonne Schalk-van der Weide werd geboren op 9 juni 1965 te Breukelen, waar zij het lager onderwijs genoot op de Schepershof (1971-1977) en het V.W.O. doorliep op de Rijksscholengemeenschap Broklede (1977-1983).
Aansluitend hierop is zij begonnen met de opleiding tot tandarts, aan de Subfaculteit Tandheelkunde, Rijksuniversiteit Utrecht, waar in juni 1988 het tandartsexamen werd afgelegd.

In augustus 1988 startte zij als assistent in opleiding bij de vakgroep Mondziekten/Kaakchirurgie en Bijzondere Tandheelkunde van de Faculteit Geneeskunde der Rijksuniversiteit Utrecht met het onderzoek bij oligodontiepatiënten, waarvan de resultaten zijn verwerkt in dit proefschrift. Daarnaast werd zij in de gelegenheid gesteld gedurende haar aanstelling cursussen te volgen op het terrein van de Bijzondere Tandheelkunde en patiëntenzorg te verrichten bij de afdeling Bijzondere Tandheelkunde van het Academisch Ziekenhuis Utrecht.

In 1991 werd een eigen tandartspraktijk te Utrecht gestart. Vanaf 1 september 1992 werd dit gecombineerd met een part-time functie bij het NIPG-TNO te Leiden. Zij is werkzaam op de Afdeling Jeugd en Gezondheid, sectie Tandzorg en Epidemiologie. Aldaar werkt zij mee aan onderzoek naar het vóórkomen van tand- en mondziekten en naar preventief tandheelkundige maatregelen.