THE PROSTHETIC MANAGEMENT OF A HYPOHIDROTIC ECTODERMAL DYSPLASIA PATIENT A CASE REPORT

JAMES M. HORI, D.D.S.

Submitted in partial fulfillment of the requirements
for a Specialty Certificate in
Pediatric Dentistry

The Oregon Health Sciences University
School of Dentistry
June 12, 1992

APPROVAL

Harold E. Howard, D.D.S.
Graduate Program Director
Pediatric Dentistry
Oregon Health Sciences University

THE PROSTHETIC MANAGEMENT OF A HYPOHIDROTIC ECTODERMAL DYSPLASIA PATIENT A CASE REPORT

ABSTRACT

A seven year old female patient with X-linked hypohidrotic ectodermal dysplasia presented to the Oregon Health Sciences University's Graduate Pediatric Dental Clinic for evaluation and treatment. A review of this condition along with the dental management of the case is presented. The case was highlighted by the prosthetic aspect of the dental treatment which emphasized the use of stainless steel crowns with welded lugs for increased clasp retention of partial dentures.

INTRODUCTION

Hypohidrotic ectodermal dysplasia is an inherited disorder that has many features of interest to the dental practitioner. These dental anomalies not only affect function, but also may have a harmful effect on the child's social development. The esthetic and prosthetic management of these patients presents a significant challenge to the dentist. The prosthetic management of a severely affected female, who is an obligate carrier of hypohidrotic ectodermal dysplasia, is described.

REVIEW OF THE LITERATURE

The syndrome of ectodermal dysplasia results from faulty ectodermal development and is characterized by an abnormal growth of the skin and its appendages. The two major forms of this syndrome are the hidrotic and the hypohidrotic types. Each type has

a separate origin and a distinct group of clinical manifestations (Rothstein and Goldman 1979).

Weech described the hydrotic form in the late 1920's (Weech 1929). The genetic transmission is autosomal dominant, affecting males and females equally. The distinguishing feature of the hypohidrotic form is that the sweat glands are not defective although the skin may be dry. At least half the individuals present with generalized hypotrichosis with total alopecia being common. The hairs of the head, eyebrows, and body are scanty and usually the outer-thirds of the brows are often missing. Other associated features include variable dystrophy of the nails, palmoplantar hyperkeratosis with a tendency for cracking of the skin, thickening of the skull and a tufting of the terminal phalanges. The teeth are usually unaffected and normal.

Hypohidrotic ectodermal dysplasia (HED) was first described by Thurnam in 1848 (Thurnam 1848) and was recognized as an X-linked disorder by Thadini in 1921 (Thadini 1921). Charles Darwin (Darwin 1893) cited Wedderburn as having found this complex in an inbreed Indian as early as 1838. Christ (Christ 1932) defined it as a "congenital ectodermal defect " in 1913. Weech (Weech 1929) in 1920 coined the term "anhidrotic ectodermal dysplasia" due to the depressed sweat gland function. Felsher (Felsher 1944) pointed out that the skin is rarely, if ever, completely anhidrotic and suggested using the adjective "hypohidrotic" as a better choice.

X linked hypohidrotic ectodermal dysplasia is expressed fully in males and partially in heterozygous female carriers. The

prevalence in the population has been assessed to between 1:10,000 and 1:100,000 live male births. (Crawford 1991)

Hypohidrotic ectodermal dysplasia or Christ-Siemens-Touraine syndrome manifests as a triad of hypodontia, hypotrichosis, and hypohidrosis is usually associated with other components resulting from defective development of structures of ectodermal origin. The diagnosis does not require all signs to be present (Sofaer 1981).

The facies of people with HED are characterized by frontal bossing, a depressed nasal bridge, and protuberant lips resulting from loss of vertical dimension secondary to anodontia or hypodontia (Reed 1970).

Hypohidrosis is the most remarkable characteristic of this disorder. "Fever of unknown origin" may present in the first year of life. Partial absence and marked aplasia of the eccrine sweat glands contributes to the inability to sweat resulting in heat intolerance with severe incapacitation and hyperpyrexea after mild exertion or even following meals (Goodman 1970).

The skin is fair, transparent, and dry due to the absence of sebaceous glands. Flexural excema is common as well as fine linear wrinkles and increased pigmentation about the eyes and mouth (Reed 1970). The palms and soles are frequently the sites of small hyperkeratoses. Fine fetal lanugo hair may persist into post-natal and adult life. After puberty, the beard is usually normal but the pubic and axillary hair is often scanty. The scalp hair is often blond, fine, stiff, and sparse giving it a spun glass appearance. The eyebrows and eyelashes are often missing (Reed 1970).

The nails are usually normal or sometimes spoonshaped (Weech 1929). The mammary glands appear to be aplastic or hypoplastic (Osbourn 1952). Flattened epidermal ridges are seen with distorted epidermal whorl patterns (Verbov 1970) and criss-cross furrowing on the fingertips and palms (Basan 1965). Lacrimal and salivary production may be reduced (Lowenburg 1942).

GROWTH AND DEVELOPMENT

Presently the study done by Clarke (1987) has served as the classic reference for this disorder. This study showed that most boys will spontaneously show an improvement in their general condition at some point from the age of one to four years. They are no longer subject to serious illness, they feed well, and they grow and develop normally. But they may remain susceptible to recurrent upper respiratory tract infections, bouts of fever, exzema, asthma, and food allergy. They may require water with meals and need artificial tears because of inadequate salivary and lacrimal secretions. They may be bothered by teasing at school and self consciousness during adolescence, but they are unlikely to become seriously ill. Heat intolerance by older boys does occur but can be dealt with by taking cool drinks and wearing wet T-shirts. Mental retardation was not a primary feature of the disease.

.Chronic obstructive airway disease may develop in male subjects who smoke and who also work in a dusty atmosphere. This is most probably caused by defective mucous production in the respiratory tree.

Most female carriers of HED are recognized by dental anomalies. However for those with normal teeth, recognition is by their abnormal pattern of sweating. Asking for symptoms of HED and looking for sparse scalp hair were found to be too subjective to identify carriers accurately. The dental and sweating signs are useful because they can be applied to female relatives to modify the recurrence risk that is given to them after the birth of even one affected child in a family. It is hoped that DNA probe analysis of the gene will permit still more accurate counseling in the future (Clarke 1987).

ORAL FINDINGS

Hypodontia or anodontia is the most striking oral finding. This is due to suppression of the dental ectoderm. The few teeth that are present may be delayed in eruption. The lips are protuberant because of the hypodontia and the resultant loss of vertical dimension (Perabo 1956).

The alveolar process does not develop in the absence of teeth and is therefore missing. Cephalometric studies by Sarnat (Sarnat 1953), however, have shown that apart from defective alveolar growth, the jaw and face otherwise develop normally.

Affected males and carrier females both consistently showed smaller mesiodistal tooth crown diameters than did unaffected persons. The frequency of missing teeth is more than ten times the one to seven percent incidence found in the normal population. This indicates that, with respect to dental manifestations, HED segregates as a highly penetrant X-linked trait that shows intermediate expression in the heterozygous female. The occasional

occurrence of completely normal or severely affected carrier females has been attributed to random inactivation of the X chromosome (Nakata 1980).

Hypodontia was more severe in males than females, and there were differences in the pattern of hypodontia between the sexes. Most notably were first premolars which were relatively protected in females but almost universally absent in males. Abnormal crown form, with the maximum diameter of the teeth being apically displaced, was noted particularly in the anterior teeth. Taurodontism was a common feature of HED (Crawford 1991).

PRENATAL DIAGNOSIS

Prenatal diagnosis of X-linked HED was previously performed by the direct histological analysis of fetal skin obtained by late second trimester fetoscopy. The recent gene mapping of the locus for the disorder to the region of Xq11-21.1 now permits the indirect prenatal diagnosis of the disorder by the method of linkage analysis, based on closely linked marker loci during the first trimester of pregnancy (Zonana 1988). The advantage to this new method of prenatal diagnosis is that it permits a diagnosis to be made by chorionic villus sample (CVS) in the first trimester of pregnancy prior to the development of affected structures. This allows for the option of early termination of an affected pregnancy. CVS is simpler and presents a lower risk to the pregnancy than does fetoscopy and multiple skin biopsies. The disadvantages to a linkage-based indirect analysis include the need to sample previously affected individuals, additional relatives, and the patient at risk. The counseling of families is difficult and complex since one is dealing

with the probabilities of an affected fetus, rather than a more definitive diagnosis based on direct observation. With linkage analysis of a CVS, the likelihood of having an affected fetus can be presented with probabilities based on the approximate 95% confidence interval (Zonana 1990).

REPORT OF CASE

Talia Jackson, a seven year old Caucasian female, presented to the Oregon Health Sciences University School of Dentistry Graduate Pediatric Dental Clinic in January 1991 for examination, evaluation, and management of her dental condition. She exhibited the typical features of hypohidrotic ectodermal dysplasia most commonly seen in severely affected males (fig. 1 and 2). Talia presented with existing dentures (fig. 3, 4, and 5) which were made by her dentist in Great Falls, Montana. Talia and her parents' main concern was that her dentures were loose and wanted to know about possible options for modifying her old denture or making a new one. Although her existing dentures were loose she was able to stabilize it with her oral musculature.

Intraoral examination (fig. 6) revealed five erupted teeth including the mandibular left permanent first molar, the mandibular left primary second molar, the mandibular left conical shaped cuspid, both maxillary second primary molars, and both partially erupted maxillary permanent first molars. Due to the age of her existing dentures as well as the presence of erupting teeth, her dentures did not fit well and could not be seated properly. The alveolar ridge on the right side was severely underdeveloped. Her palate was broad, flat, and slightly red (Fig. 7).

A radiographic examination (fig. 8) revealed permanent maxillary first molars partially erupted. Because of the absence of teeth, only basal bone developed in the right side of the mandible.

FAMILY HISTORY

Hypohidrotic ectodermal dysplasia has been transmitted in the Jackson family through three generations (fig. 9). Joyce, the grandmother, is a phenotypically normal carrier. All of Joyce's brothers were affected and one of them has one nipple missing. Timothy, the father (fig. 10), is hemizygous and has had anodontia in both deciduous and permanent dentitions. His other HED characteristics include a depressed nasal bridge, frontal bossing, and an inability to sweat. All his daughters show the phenotype of the disease. However, the degree of expression is varied from one daughter to another because of random inactivation of the X chromosome. Talia, Tara, and Shaina are triplets with Talia and Tara being identical. Alisa is the oldest sister.

Talia Jackson, triplet A, was born on 6/19/83 at 33 1/2 weeks gestation. Her birth weight was 1.3 kilograms. She and her sister Tara were monochorionic triplets. Talia is the most affected of all her sisters and has the greatest heat intolerance while sweating very little. She has managed to cope with this by staying out of the sun and by sometimes wearing a wet shirt over herself. The hair on her head is thin, and she has very little hair on her arms and legs. Midface hypoplasia is noticeable with a low nasal bridge and small nose. She has seven natural teeth and wears partial dentures.

Tara Jackson, triplet B, was monochorionic with her sister Talia. She weighed 1.4 kilograms at birth. She is not bothered much

by the heat, and sweats a little less than normal. Tara has sparse hair on her arms, but leg hair is normal, as is the hair on her head. She has 14 teeth but is missing ten and therefore has had to wear partial dentures.

Shaina Jackson, triplet C, was most probably a fraternal sibling of Talia and Tara. She was larger at birth than her sisters and appears to be the least affected. Shaina has no heat intolerance and sweats normally. She has a thick head of hair and good hair distribution elsewhere. She has all her teeth but they are conical in shape.

Alisa Jackson, the oldest sister, was born on 10/17/80 by vaginal delivery with forceps at term. She suffers from asthma and eczema which is manifested facially. She is near-sighted. She has no noticeable heat intolerance and is noted to sweat on the back of her neck. Alisa has hair on her legs none on her arms, and the skin on her checks is dry. She is missing three teeth.

Tim Jackson, the father, was diagnosed at a very young age with hypohidrotic ectodermal dysplasia. He has been anodontic throughout his life and wears complete upper and lower dentures. He does not sweat at all and must wear wet t-shirts to keep himself cool in hot temperatures. He has always had thin hair and is predominantly bald except for the sides of his head. He has no hair on his arms or legs but does have facial hair. He has some noticeable midface hypoplasia with frontal bossing and a depressed nasal bridge.

Joyce Ogden, the paternal grandmother, has no intolerance to heat and does sweat. She recalls being told she had missing teeth

by her dentist when she was young. Joyce appears normal but is missing three teeth.

PROSTHETIC MANAGEMENT

Diagnostic impressions were made using irreversible hydrocolloid impression material in a stock tray and casts were poured in yellow stone. The casts reemphasized the poor development of the right mandibular ridge. The maxilla was not as severely underdeveloped.

In order to increase retention of these partial dentures, stainless steel crowns with welded horizontal buccal lugs were planned. Standard Unitek (Unitek/3M, Monrovia, California) stainless steel crowns were fitted on teeth #'s A, J, and K, the maxillary left and right primary second molars and the mandibular left second primary molar (fig. 11 and 12). The crown preparation consisted of minimal proximal reduction due to the conical shape and almost no occlusal reduction in order to increase her vertical dimension. A 0.045 Blue Elgiloy wire was adapted and welded to the buccal surface of the crowns thus creating an undercut for clasp engagement to increase the retention. The crowns were then crimped, polished, and cemented with glass ionomer cement.

Custom acrylic resin impression trays were made on the diagnostic casts and then used to obtain final impressions utilizing irreversible hydrocolloid. Occlusal rims were made using orthodontic acrylic from the master casts and then built up with baseplate wax. A bite registration was taken using Aluwax (Aluwax, Grand Rapids, Michigan), the maxillary midline was marked, and the casts mounted on a Hanau (Teledyne Hanau, Buffalo, New York)

articulator. The maxillary anterior teeth were set and tried-in the patient. During the anterior try-in, it was determined that the lip support was inadequate. Therefore the teeth were repositioned about one millimeter labially, the vertical dimension was arbitrarily opened two millimeters, and the remaining teeth were set to this new position.

The final wax try-in was quite acceptable. The bite was stable in centric relation and had balanced occlusion in lateral and protrusive movements. Adequate lip support was attained. The patient indicated that she was very happy with the esthetics and function.

Clasps were constructed using 0.045 Blue Elgiloy wire because they are reported to be more resilient and durable than a stainless steel wire. The maxillary clasps were designed to go around the permanent molar, continuing to the vestibule, and then engage under the buccal lug on the crowns from the distal going mesial to the lug about four to five millimeters. The clasps then ended in a lump of solder that functions as a handle for the patient to engage and disengage the clasp. Maximum length was desirable because it provides more flexibility to the clasp and was easier to adjust. This clasp design also allows the partially erupted maxillary molars to erupt without interference (Ridgley 1991). The clasps were placed on the master cast and covered with wax to the proper extension of the denture. The final festooning was completed and sent to the dental laboratory for heat cure processing (fig. 13-16).

At the delivery appointment (fig. 17-21), the buccal of the maxillary anterior and the mandibular retromylohyoid region of the

partial dentures were ground out due to inability to seat the denture properly and the patients' comfort. The clasps were adjusted and then pumice and high shine were used to polish. Post insertion evaluation confirmed that the bite was stable in centric relation. Protrusive and lateral movements were balanced thus providing adequate stability.

At the 48-hour check, ulcerations were found in the maxillary frenum and incisive foramen areas. PIP paste (Mizzy, Clifton Forge, Virginia) was used and pressure spots were slightly relieved.

The patient was very pleased with her new denture's esthetics (fig. 22 and 23). She was able to smile naturally, and appeared much happier. Talia has been enjoying an unrestricted diet that includes corn on the cob even though it was not recommended. On returning for her six month recall, the clasps had caused indentations on the gingiva but these remained asymptomatic. Esthetics and function were judged very adequate.

DISCUSSION

One of the major problems encountered with hypohidrotic ectodermal dysplasia stems from the inability to sweat, which makes it difficult for the patient to tolerate a warm environment. The psychological impact of the disorder on child and parents is another problem. Little can be done for many of the general facial characteristics, but appearance can be greatly enhanced by restoring the vertical dimension and providing an esthetically acceptable dentition. This is especially important when the child is subjected to peer evaluation. The child who appears "different" to his/her

peers may suffer ridicule and rejection and may have difficulty socializing (Geopferd 1981).

It has been noted that dental restorations can have a major impact on a person's psychological well-being. A child needs to feel adequate and competent while given social approval along with a sense of status and belonging. These drives are tested in the child when he starts school. Since children with ectodermal dysplasia are generally of normal intelligence, they soon leave the security of home and go to school. This can result in a potentially stressful situation that can influence the child's whole outlook on life. Frustration may ensue if the child feels that his appearance is a major obstacle to his appearance and self esteem. Early prosthodontic consultation is therefore an essential part of the management of ectodermal dysplasia (Grieder 1973).

Prosthetic treatment of ectodermal dysplasia rarely has been reported in the literature. Nortje (Nortje 1978) treated a patient with two incisiform teeth with an overdenture. Geopferd (Geopferd 1981) used a combination of orthodontics to position the teeth, composite to build up the conical teeth, a maxillary fixed partial denture, and a mandibular complete denture.

There appears to be little in the way of adequate statistics as to the effect of the dentures on growth and development of the jaws. Histologically there seems to be no essential difference between so-called "basal bone" and the bone normally found supporting the teeth. It is apparent from studies of residual ridge resorption in persons rendered edentulous that more than two thirds of original mandibular height may occasionally be resorbed, especially in

persons with a low calcium intake in their diet or other predisposing factors. Although resorption of "basal bone" can occur under dental prosthesis, it is not clear whether this applies to young persons on an adequate diet when the edentulous state is related to agenesis of teeth rather than dental extractions. It is felt that the psychological benefits that accrue from prostheses will outweigh any resultant bone loss (Wical 1974).

Sarnat and associates (Sarnat 1953) have emphasized the need for regular adjustments to and replacement of dentures used by the growing child. For their patient with ectodermal dysplasia they constructed five sets of dentures in the ten year period from six to 16 years of age.

Since our patient had only five teeth present consisting of three deciduous and two permanent, with two permanent molars partially erupting; a maxillary and mandibular partial denture with clasps would be the treatment of choice. A seven-year old who is still growing will require regular adjustments and replacements will be needed in the future. These dentures will need to be replaced about every two years with regular adjustments as needed (Sarnat 1953).

Looking at the long term treatment plan when the patient has definitely stopped growing, a more definitive treatment plan should be considered such as the use of implants with a fixed denture. Ekstrand (Ekstrand 1988) reported that an acceptable solution was obtained by osseointegrated implants. The patient received maxillary and mandibular removable dentures at 20 years of age and had another one remade three years later. Titanium fixtures of the

Branemark type were placed in the mandible (Branemark 1977). Five implants were placed in the mandible as abutments for a fixed bridge. This fixed bridge has now been functioning satisfactorily six months later.

CONCLUSION

Hypohidrotic ectodermal dysplasia is an inherited disorder that presents the dentist as a two-fold problem. The dental practitioner must not only restore the patients function but also esthetics. In order to prevent and/or minimize some of the psychological ramifications that may affect the appearance of the child, treatment should be initiated before the child begins school. The clinical management of a similarly affected child should consist of removable dentures which will need to be adjusted regularly and remade as needed. The use of clasps that engage in the undercut created by the lug on the stainless steel crown is effective in increasing the retention of the dentures. After the patient's growth ceases, the long term treatment plan should include the consideration of osseointegrated implants to stabilize a denture or a fixed bridge.

BIBLIOGRAPHY

Basan M. Ektodermale dysplasie. Arch Klin Exp Dermatol 1965; 222: 546-557.

Branemark P.-J, Hansson B.O., Adell, R. et al. Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. Stockholm: Almquist-Wiksell, 1977.

Christ J., Uber die Korrelationen der kongenitalen Defekte des Ektoderms untereinander, mit besonderer Berucksich-tigung ihrer Beziehunngen zum Auge. Zentralbl. Haut Geschlechtskr 1932;40:1-21.

Clarke A., Phillips D I M., Brown R., and Harper P S. Clinical aspects of X-linked hypohidrotic ectodermal dysplasia. Arch Dis Child 1987; 62:989-996.

Crawford P., Aldred M., Clarke A. Clinical and radiographic dental findings in X linked hypohidrotic ectodermal dysplasia. J Med Genet 1991;28:181-185.

Darwin C. The Variations of Plants and Animals under Domestication, Appleton, New York, 1893; 2:319.

Ekstrand K., Thomsson M. Ectodermal dysplasia with partial anodontia: prosthetic treatment with implant fixed prosthesis. J Dent Child 1988; July-August:282-284.

Felsher Z. Hereditary Ectodermal Dysplasia. Report of a Case with Experimental Study. Arch Dermatol Syph 1944;78:410-414.

Goepferd S., Carroll C. Hypohidrotic ectodermal dysplasia: a unique approach to esthetic and prosthetic management. J Am Dent Assoc 1981;102:867-869.

Goodman R., Gorlin R. Atlas of the face in genetic disorders, ed 2. St. Louis, C. V. Mosby Co., 1977, p 382.

Goodship J., Malcolm S., Clarke A., Pembrey M. Possible genetic heterogeneity in X linked hypohidrotic ectodermal dysplasia. J Med Genet 1990;27:422-425.

Grider A. Psychologic aspects of prosthodontics. J Prosthet Dent 1973;30:736.

Nakata M, Koshiba H, Eto K., Nance W. A Genetic Study of Anodontia in X-Linked Hypohidrotic Ectodermal Dysplasia. Am J Hum Genet 1980;32:908-919.

Nortje C., Farman A., Thomas C., Dent H., Watermeyer G. X-linked hypohidrotic ectodermal dysplasia-An unusual prosthetic problem. J Prosthet Dent 1978;40:137-142.

Norval E., et al. Hypohidrotic Ectodermal Dysplasia: A Genealogic, Stereomicroscope, and Scanning Electron Microscope Study. Pediatr Dermatol 1988;5:159-166.

Osbourn R. Congenital Ectodermal Dysplasia with Amastia. J Am Med Assoc 1952;148:644-645.

Perabo F., et al. Ektodermale Dysplasie von anhidrotischen typus. Helv Paediatr Acta l956;11:604-639.

Reed W., et al. Clinical Spectrum of Anhidrotic Ectodermal Dysplasia. Arch Dermatol 1970;102:134-143.

Ridgley, Patricia. Personal interview. The design and properties of a 0.045 Blue Elgiloy wire clasp. 1991.

Rothstein S., Goldman H. Hypohidrotic Ectodermal Dysplasia: A Case Report. J Oral Med 1979;34:73-75.

Saksena S., Bixler D. Facial Morphometrics in the Identification of Gene Carriers of X-Linked Hypohidrotic Ectodermal Dysplasia. Am J Med Genet 1990;35:105-114.

Sarnat B., et al. Fourteen Year Report of Facial Growth in Case of Complete Anodontia with Ectodermal Dysplasia. Am J Dis Child 1953;86:162-169.

Sofaer J. Hypodontia and sweat pore counts in detecting carriers of X.linked hypohidrotic ectodermal dysplasia. Br Dent J 1981;151: 327-330.

Thurnam J. Two cases in which the skin, hair, and teeth were very imperfectly developed. Proc R Med Chir Soc (Lond) 1848;31:71-82.

Thadini K. A toothless type of man. J Hered 1921;12:87-8.

Verbov J. Hypohidrotic Ectodermal Dysplasia: An Appraisal of Diagnostic Methods. Br J Dermatol 1970;83:341-348.

Weech A. Hereditary Ectodermal Dysplasia. Am J Dis Child 1929;37: 766-790.

Wical K., Swoope C. Studies of residual ridge resorption Part II. The relationship of dietary calcium and phosphorus to residual ridge resorption. J Prosthet Dent 1974;32:13.

Zonana J., et al.: X-linked Hypohidrotic Ectodermal Dysplasia: Localization within the Region Xq11-21.1 by Linkage Analysis and Implications for Carrier Detection and Prenatal Diagnosis. Am J Hum Genet 1988;43:075-085.

Zonana J., et al.: Prenatal Diagnosis of X-Linked Hypohidrotic Ectodermal Dysplasia by Linkage Analysis. Am J Med Genet 1990;35: 132-135.

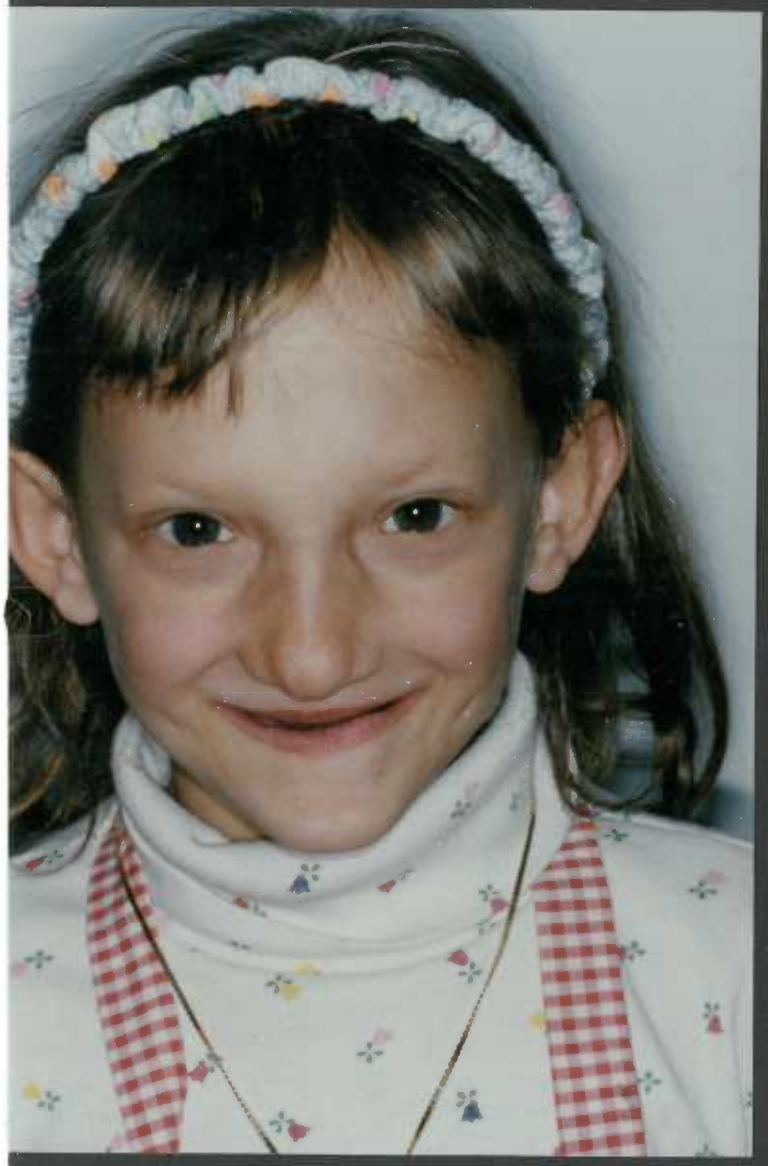

Fig. 1

Fig. 2

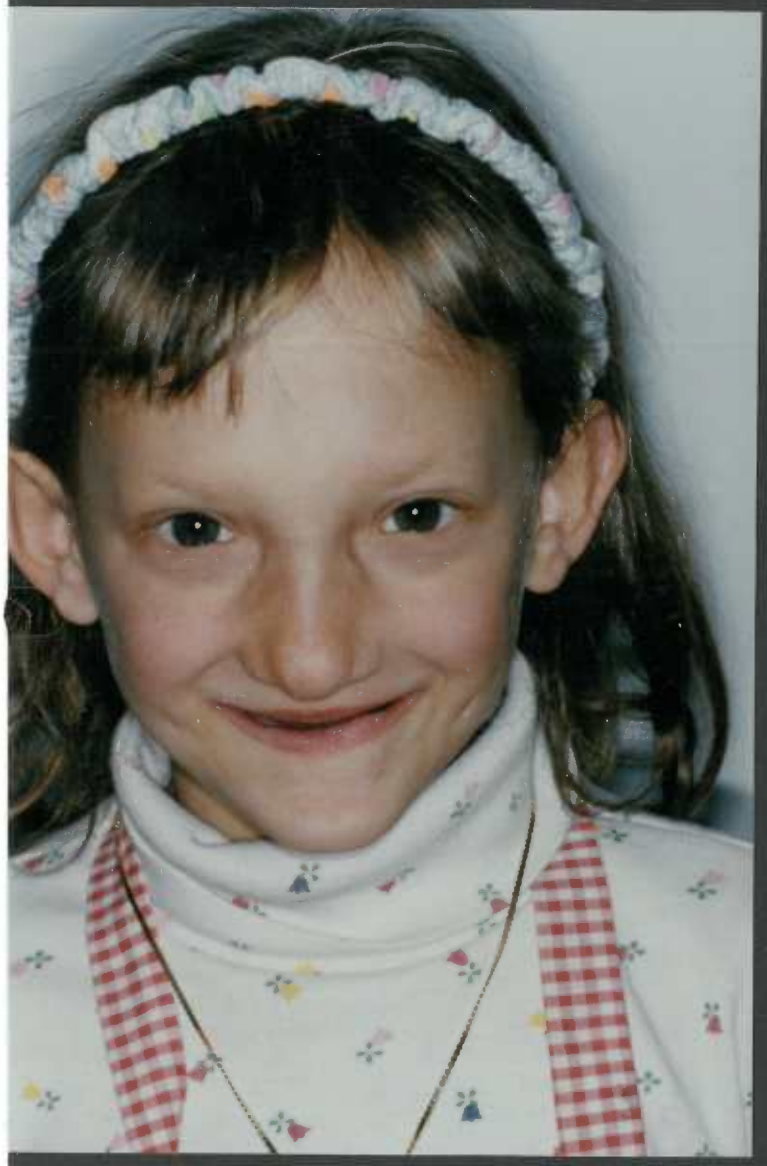

Fig. 1

Fig. 2

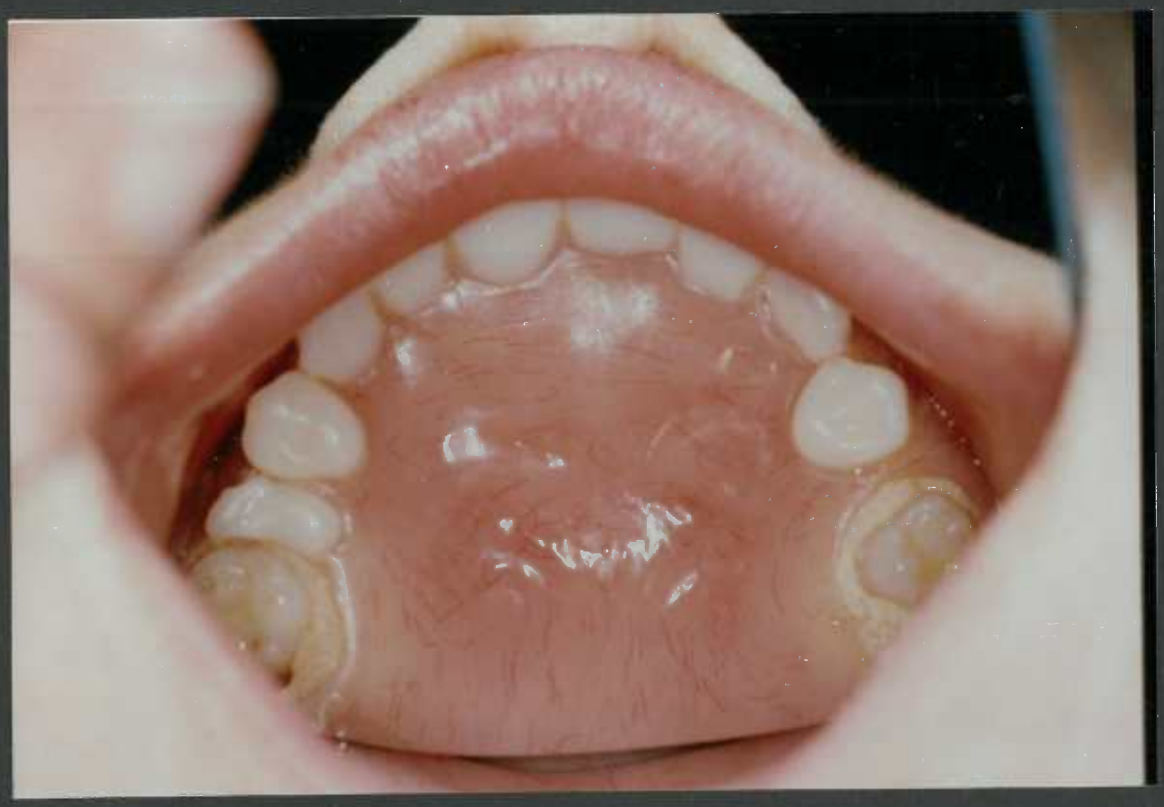

Fig. 3

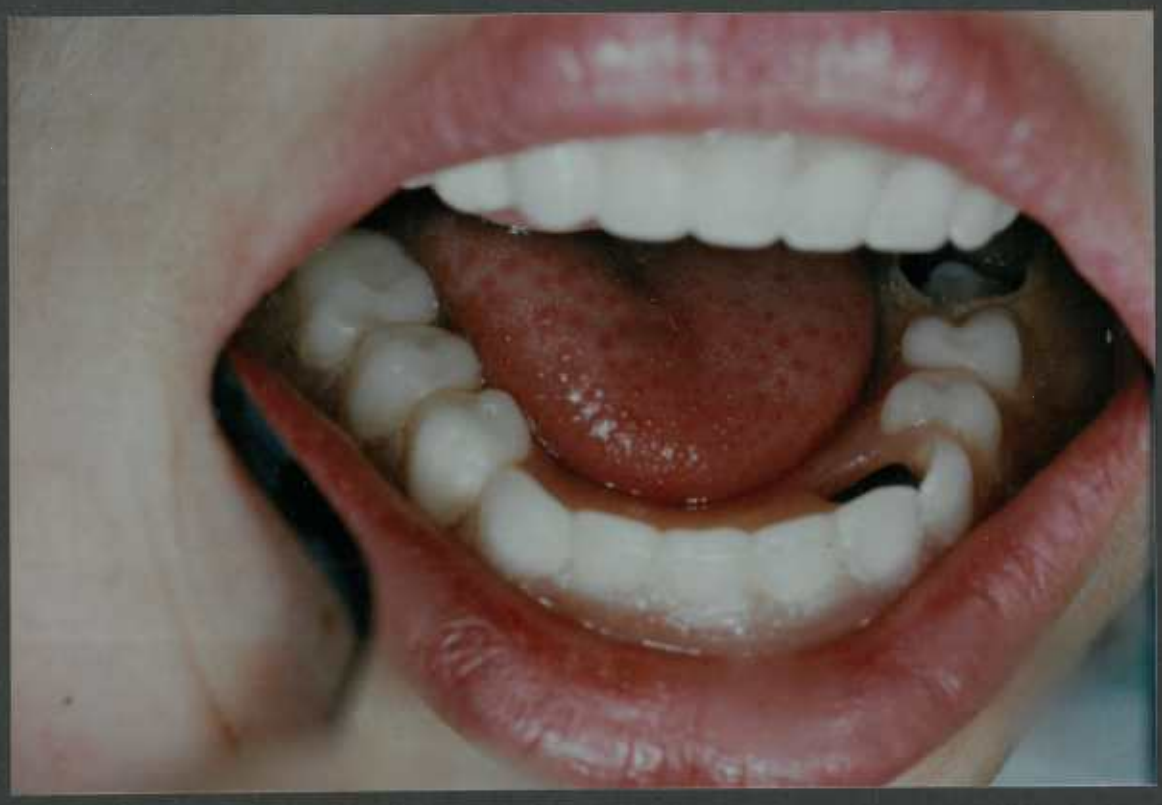

Fig. 4

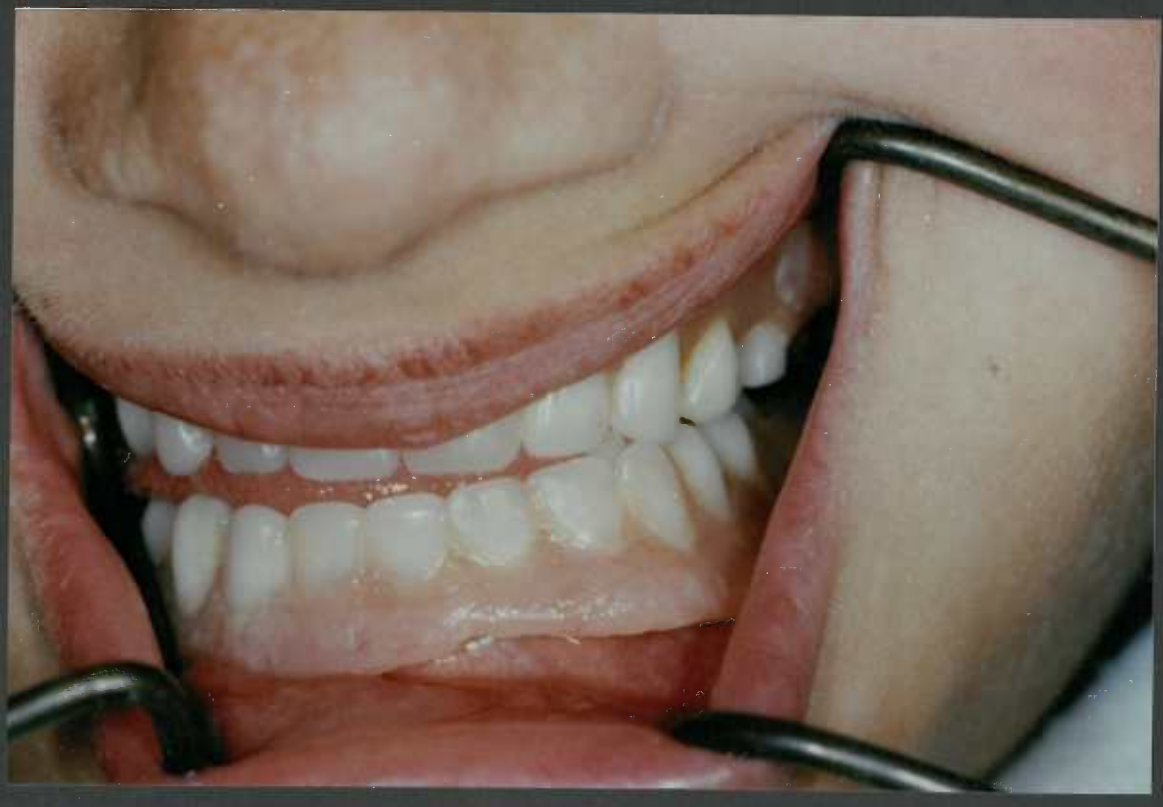

Fig. 5

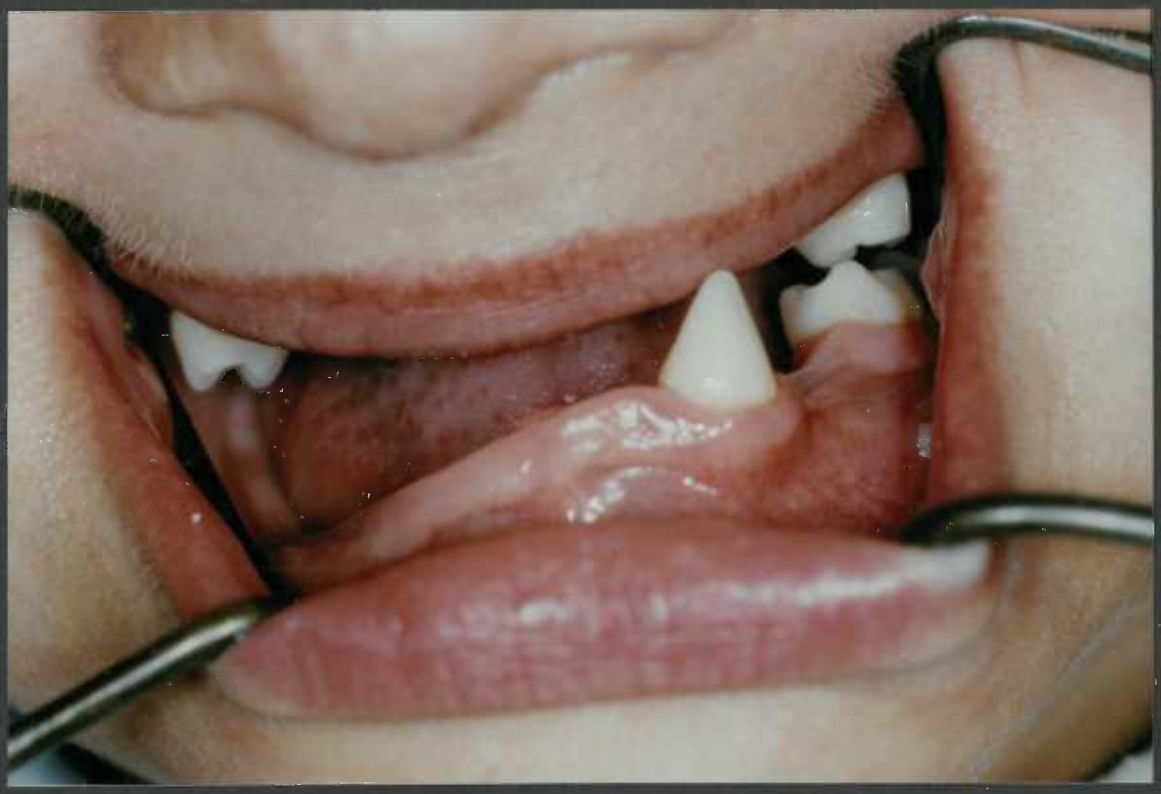

Fig. 6

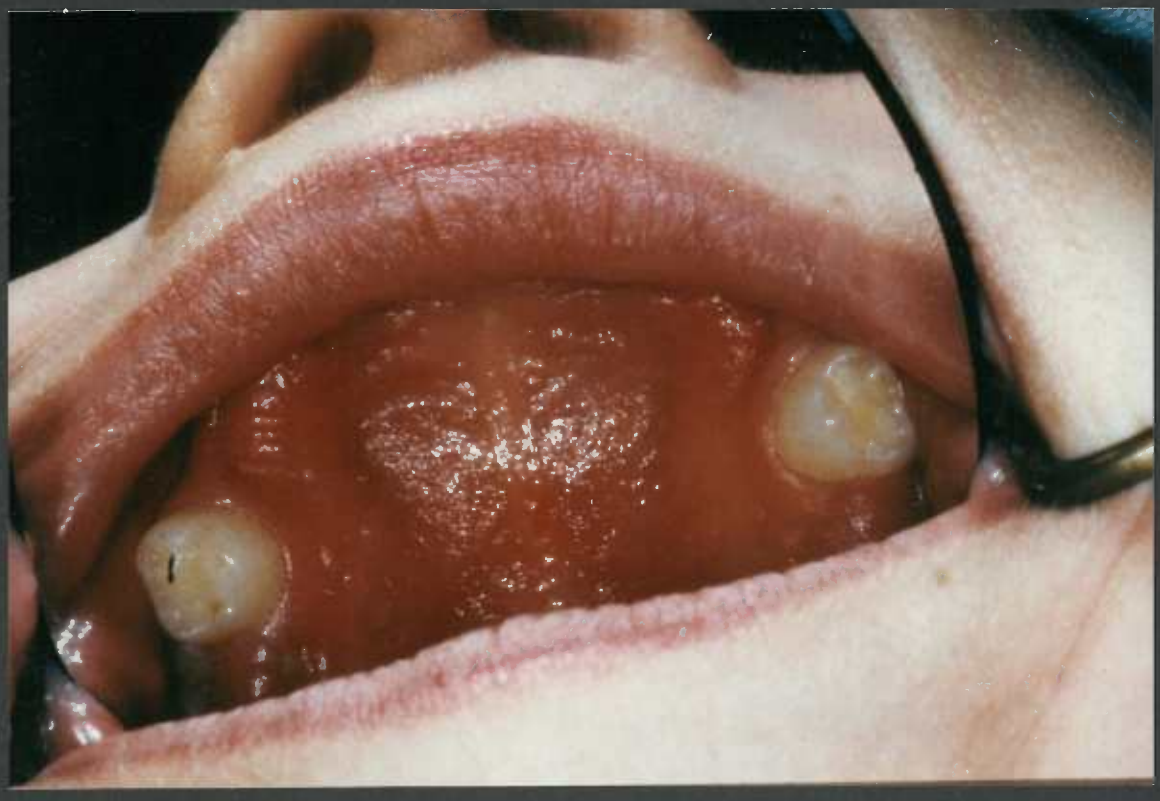

Fig. 7

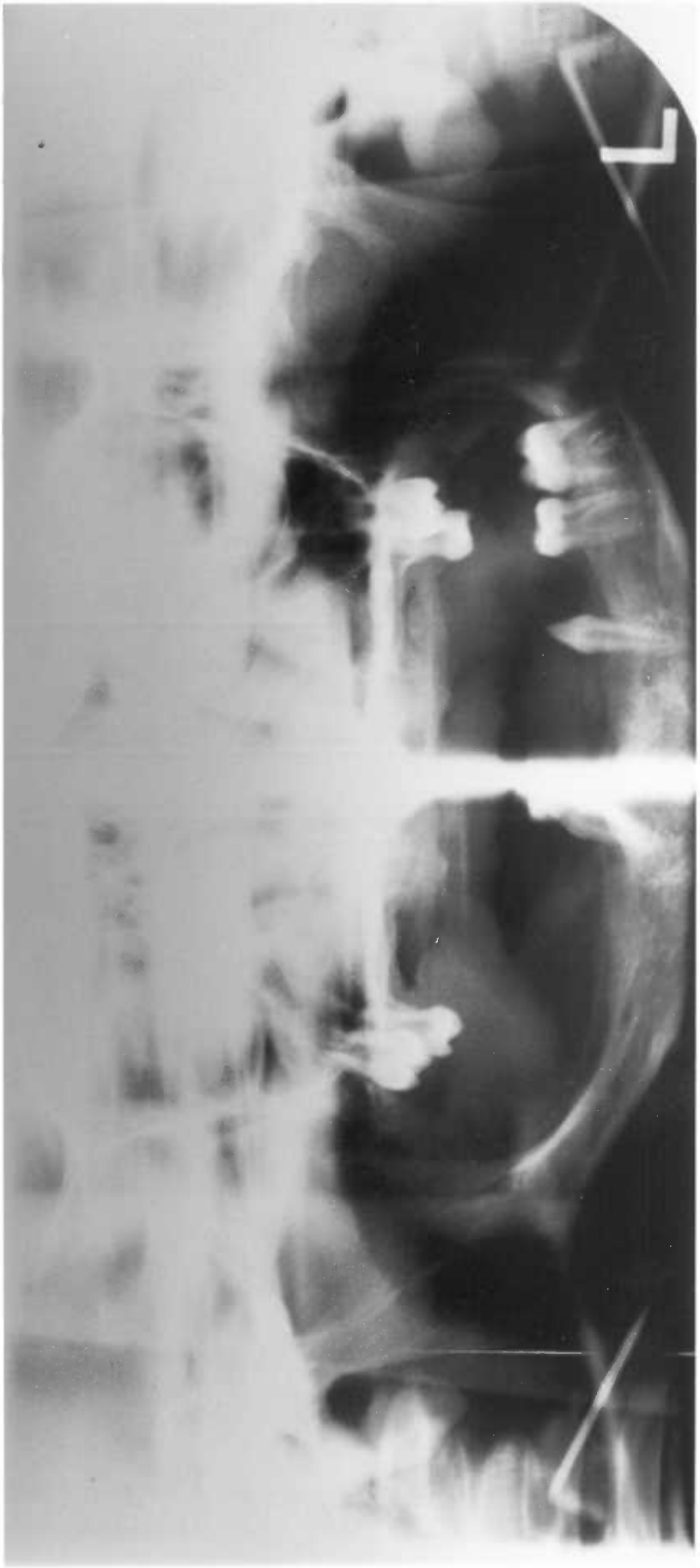

Fig. 8

Jackson Family Pedigree

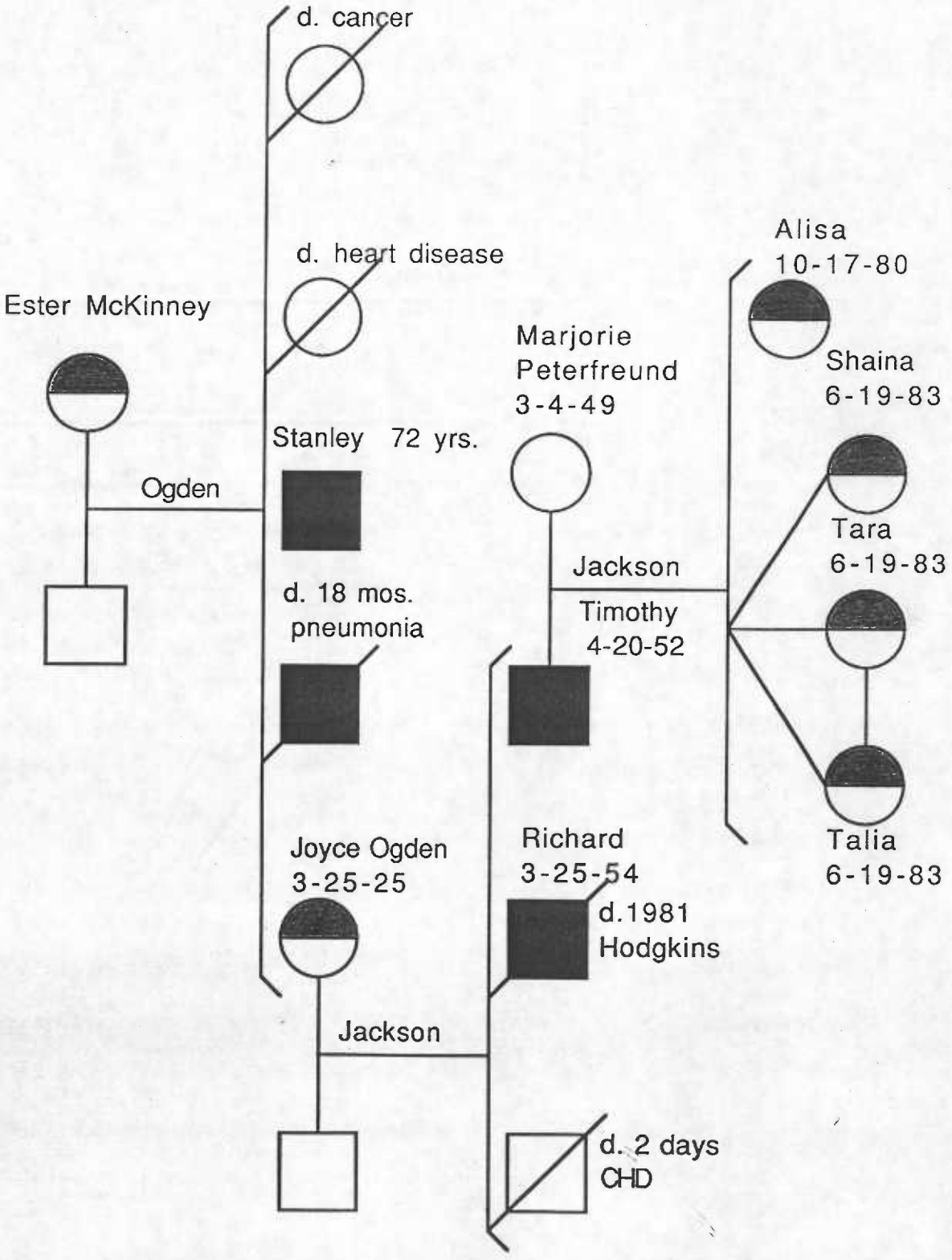

Fig. 9

Fig. 10

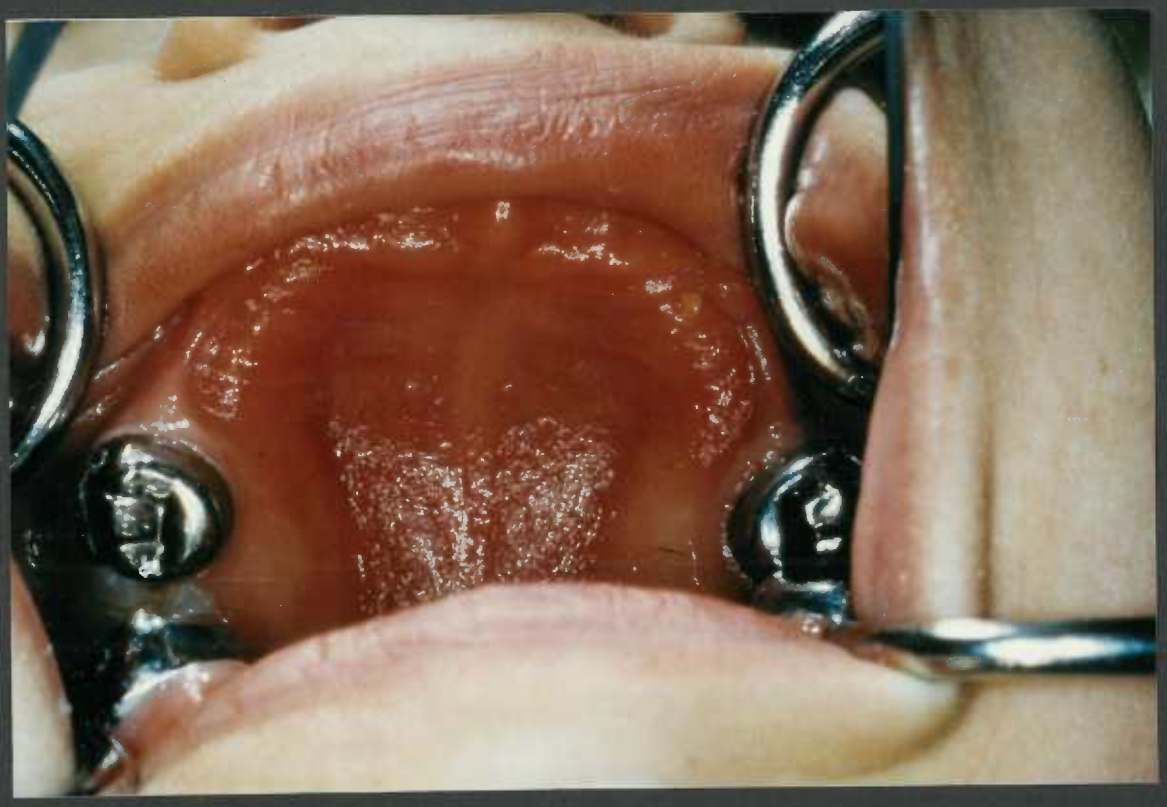

Fig. 11

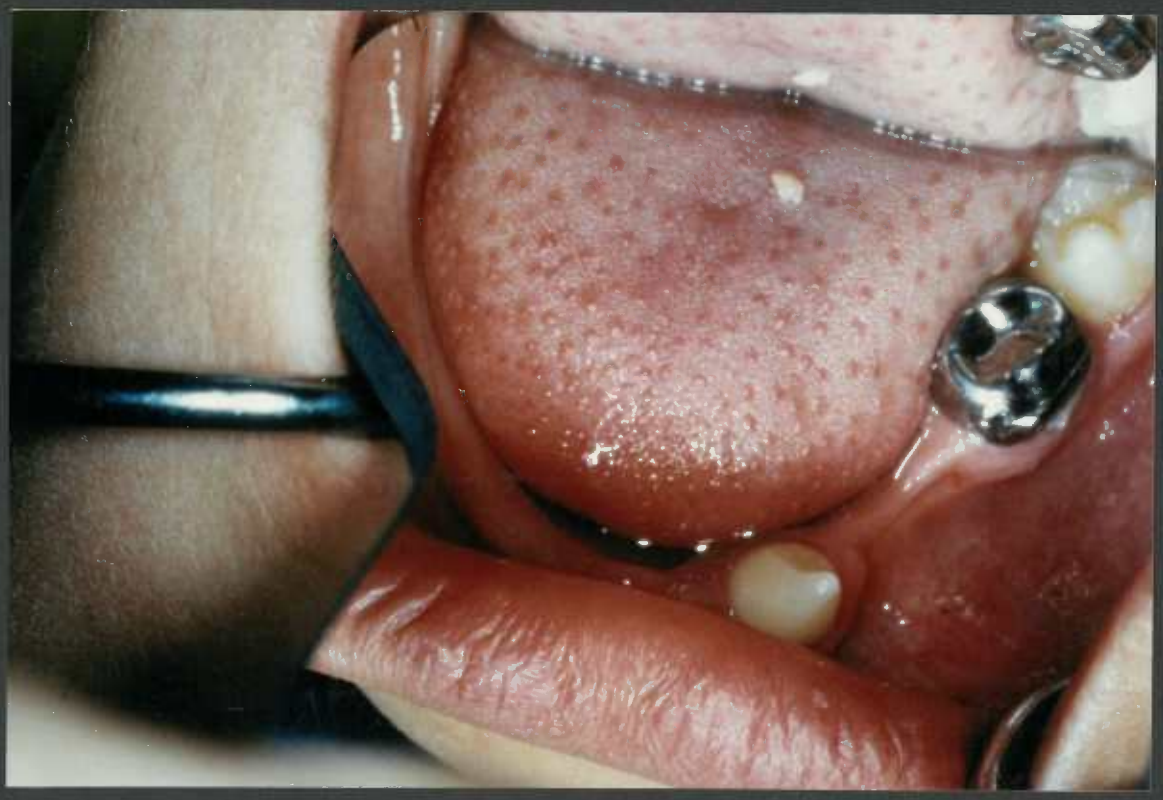

Fig. 12

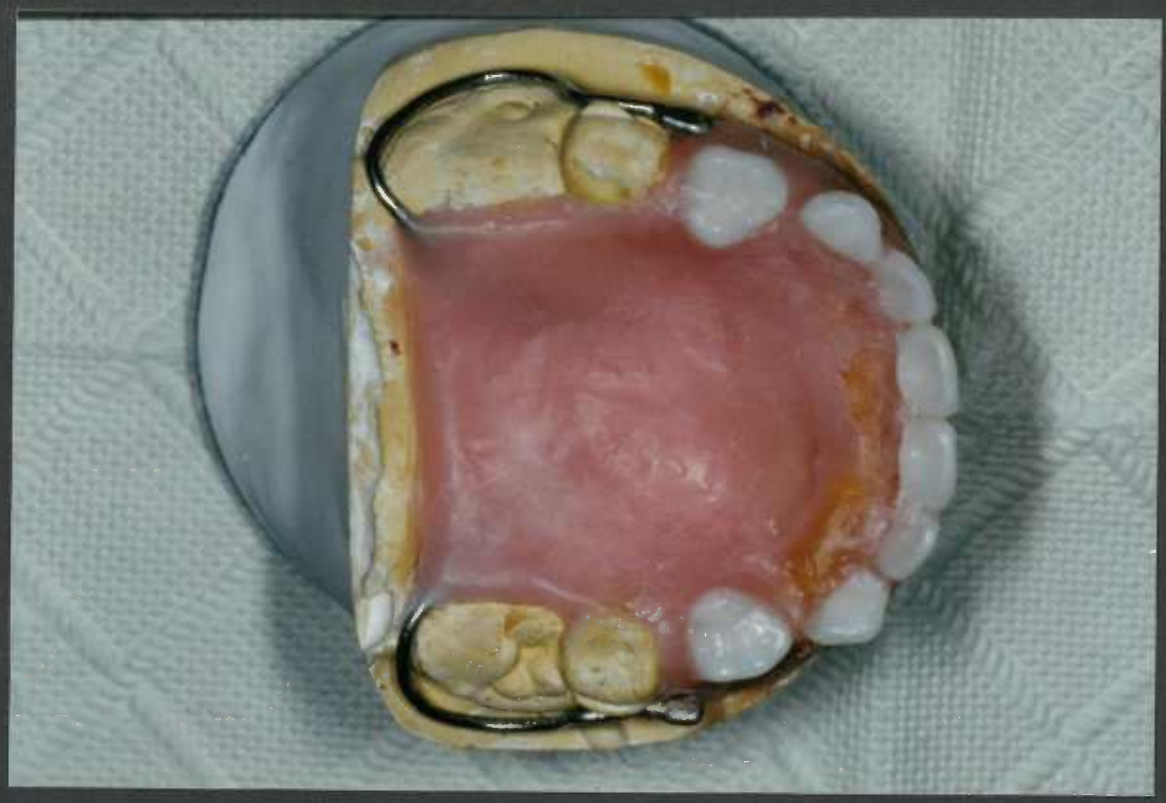

Fig. 13

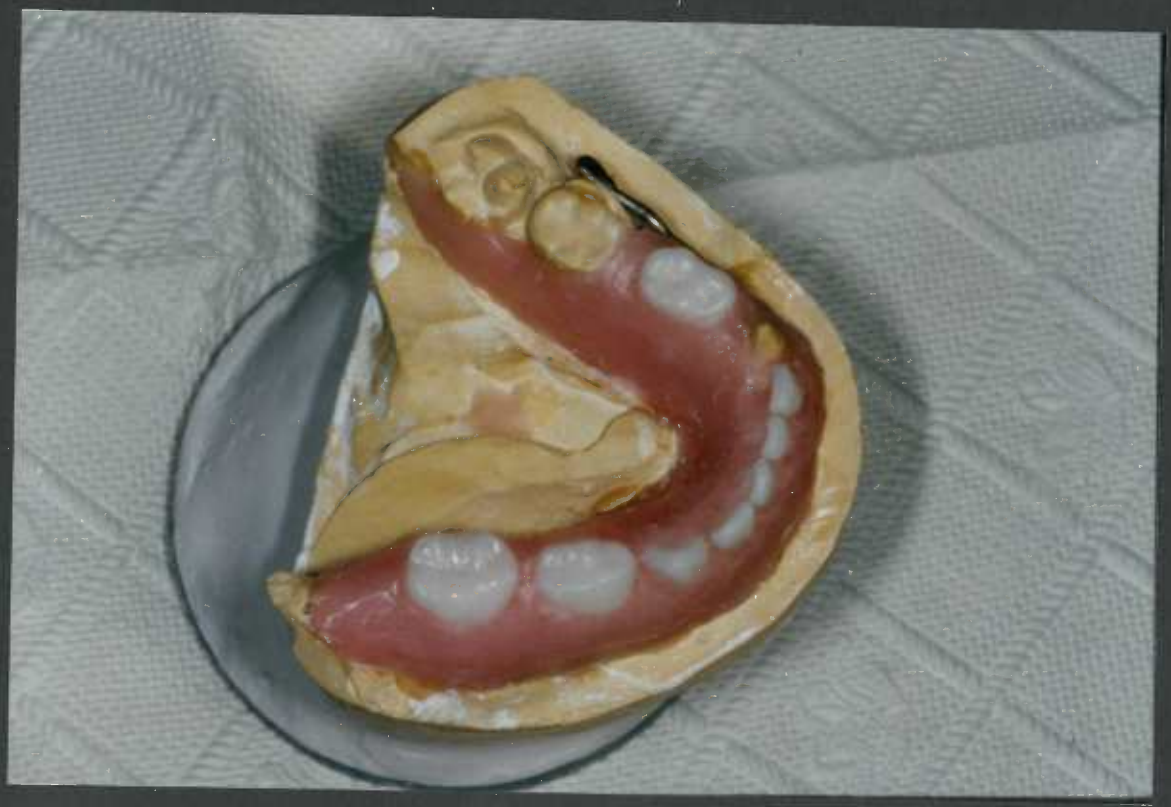

Fig. 14

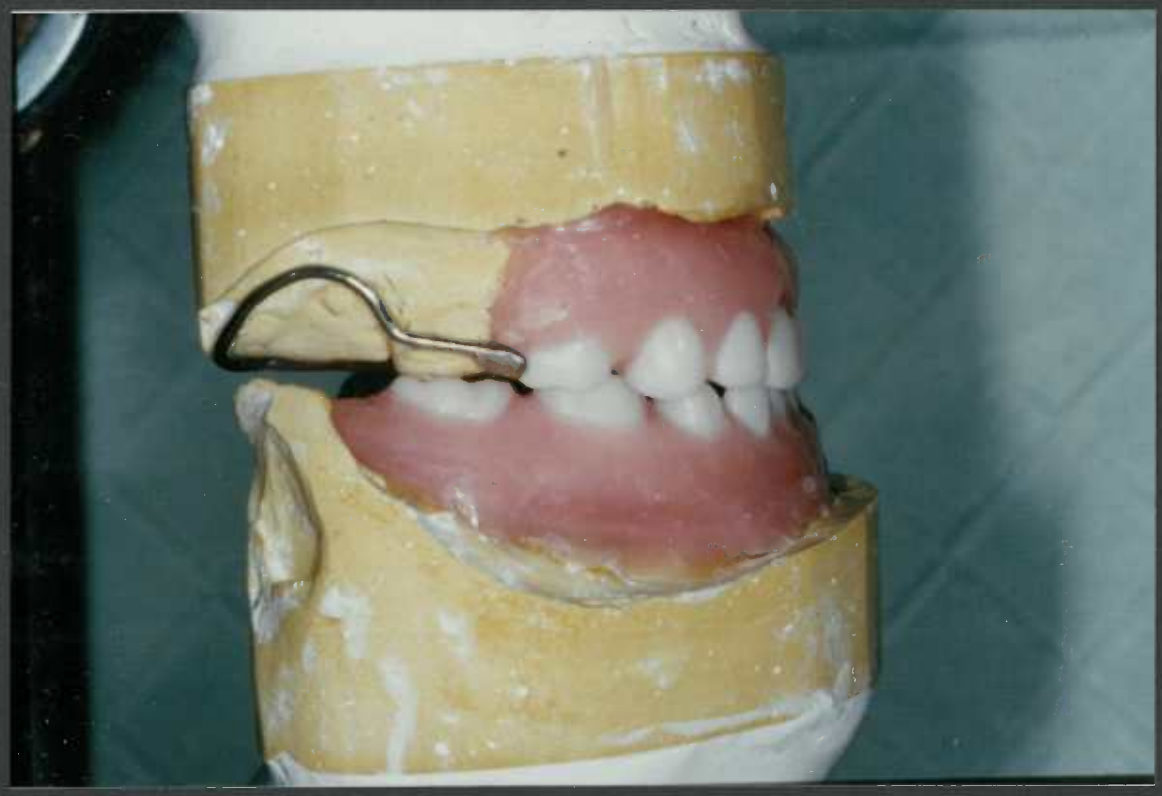

Fig. 15

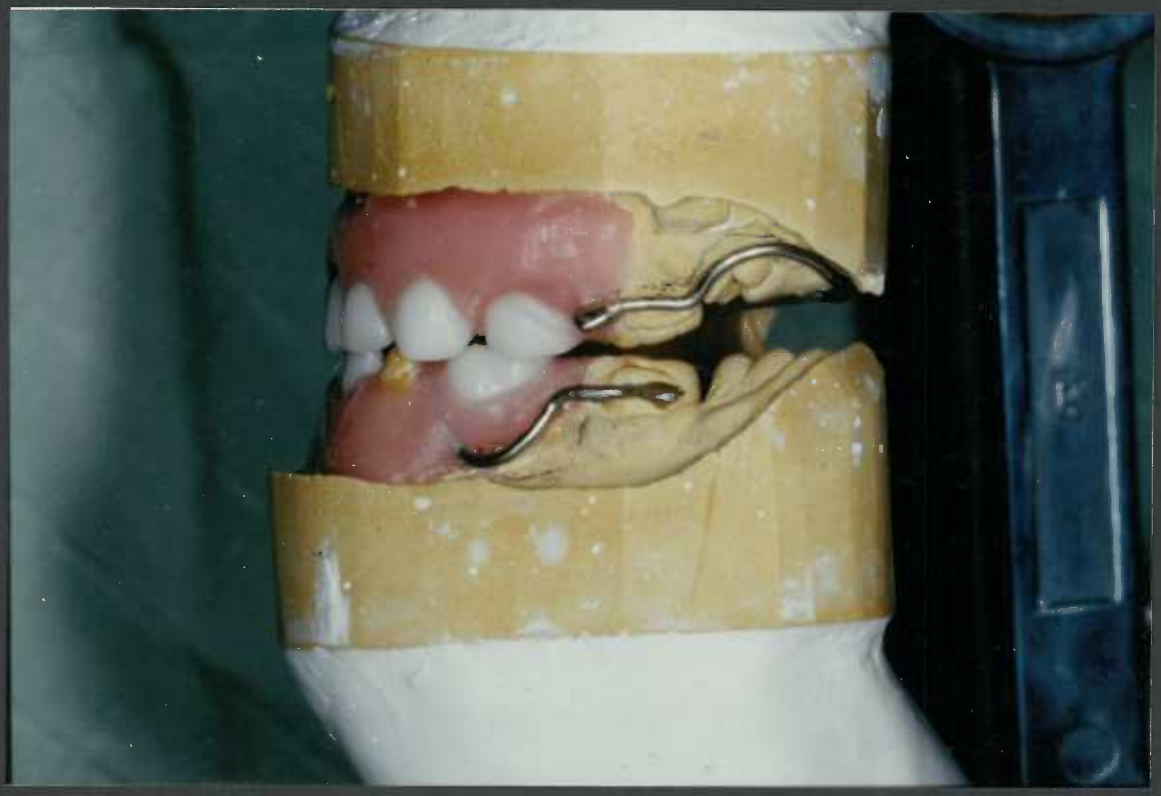

Fig. 16

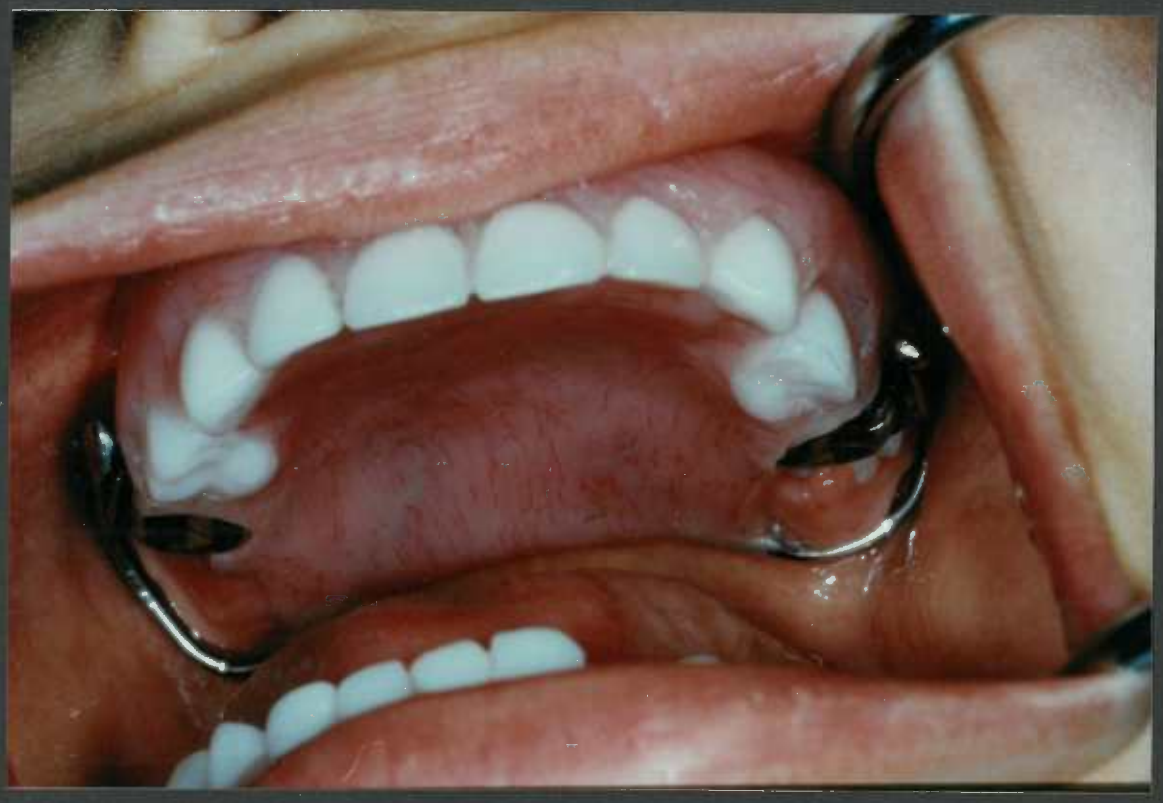

Fig. 17

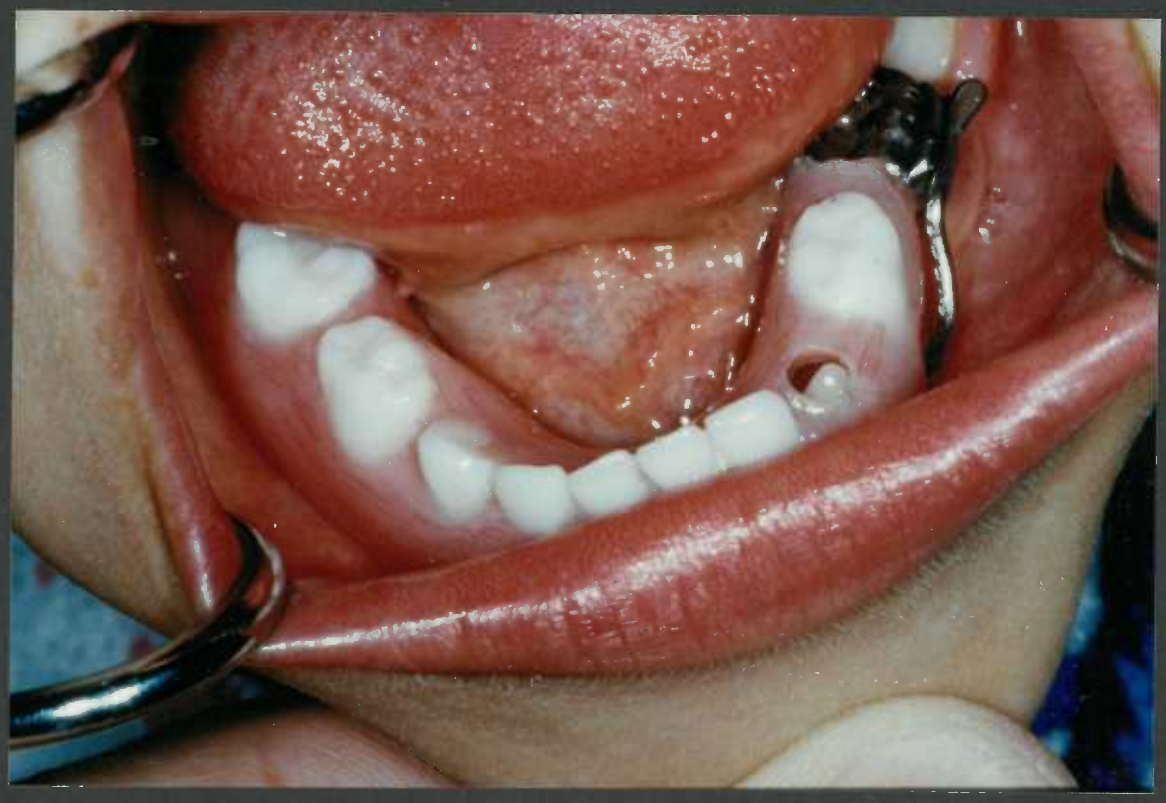

Fig. 18

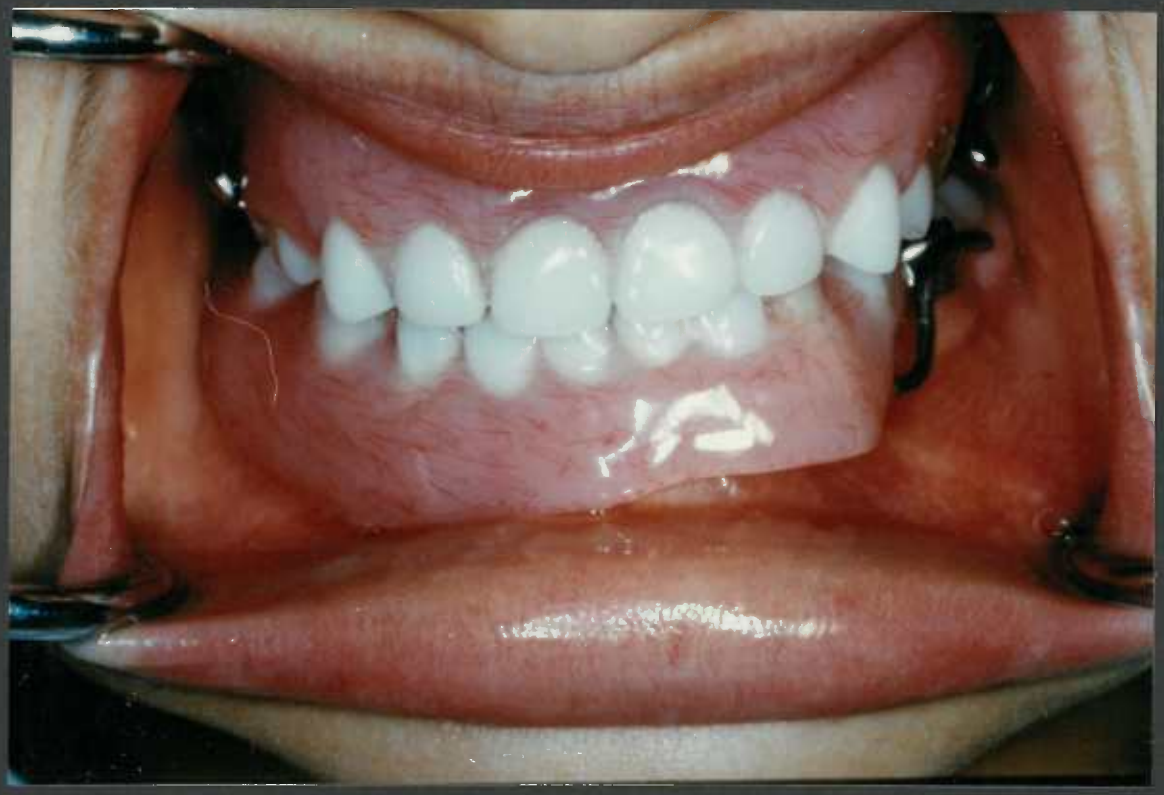

Fig. 19

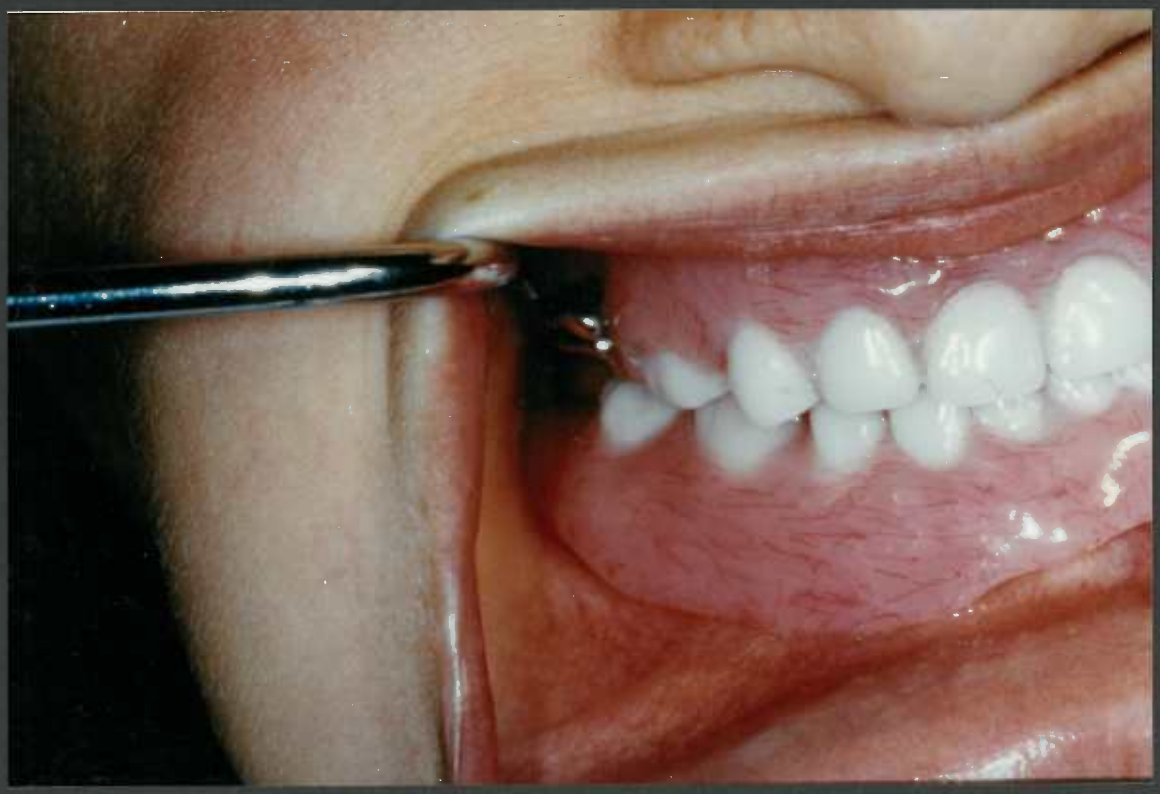

Fig. 20

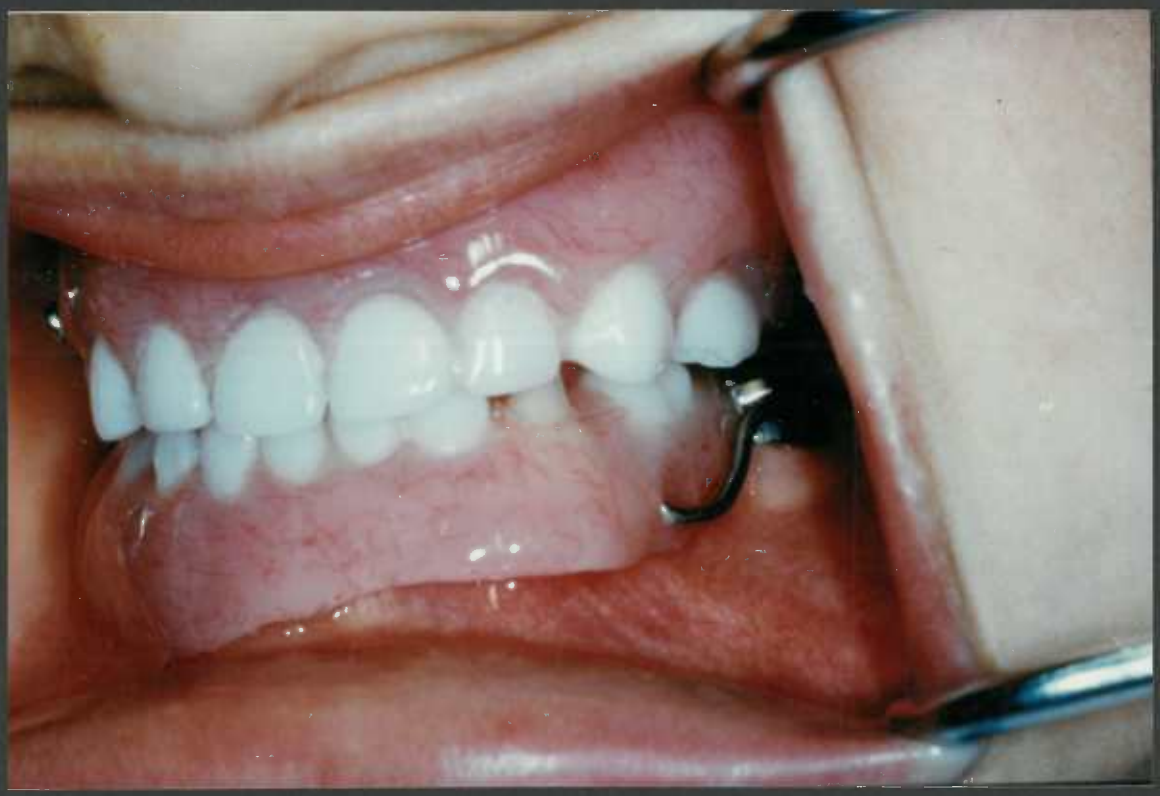

Fig. 21

Fig. 22

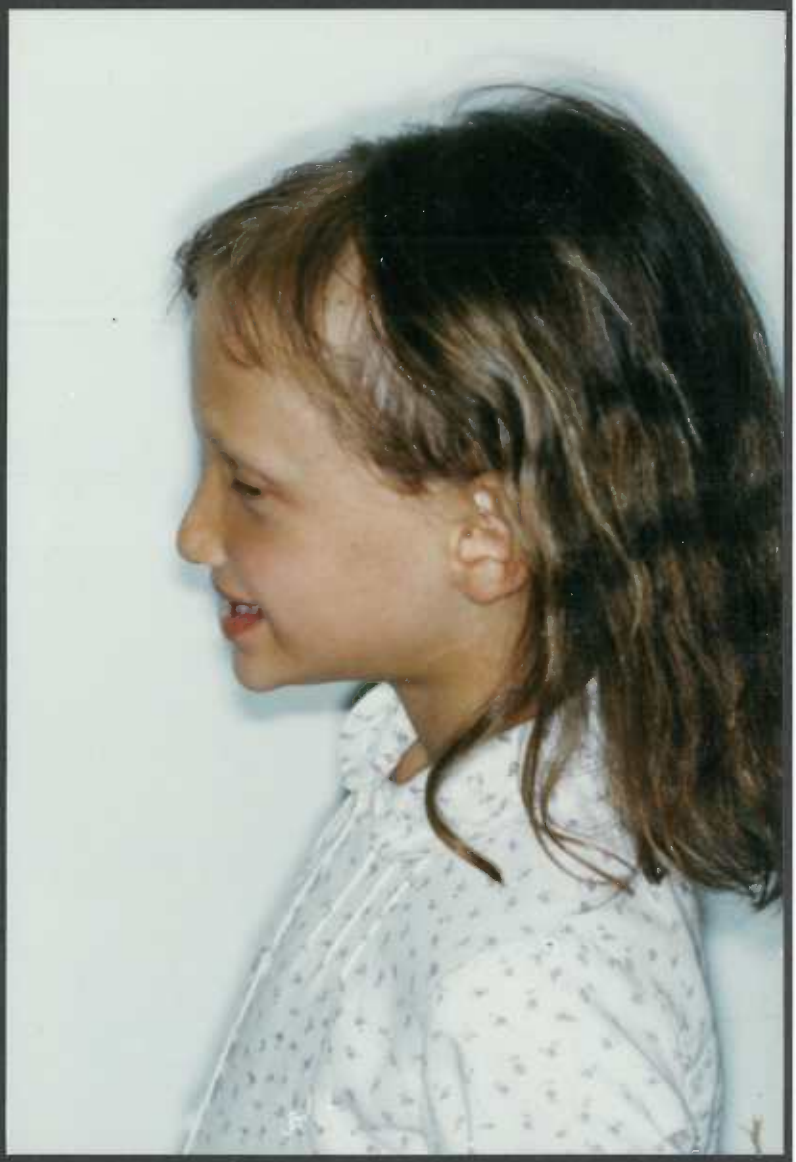

Fig. 23